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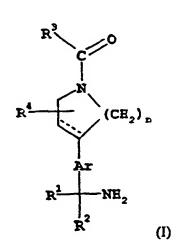
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(54) Title: ARYLMETHYLAMINE DERIVATIVES FOR USE AS TRYPTASE INHIBITORS



(57) Abstract: Provided herein are compounds of formula (I) wherein R¹⁻⁴, n and Ar are as defined in claim 1, and their pharmaceutical compositions. These compounds are tryptase inhibitors and may be used in the treatment of e.g. asthma and inflammatory diseases.

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ARYLMETHYLAMINE DERIVATIVES FOR USE AS TRYPTASE INHIBITORS

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FIELD OF THE INVENTION

This invention is directed to substituted arylmethylamines, their preparation, pharmaceutical compositions containing these compounds, and their pharmaceutical use in the treatment of disease states capable of being modulated by the inhibition of tryptase.

BACKGROUND OF THE INVENTION

Tryptase is stored in mast cell secretory granules and is the major secretory protease of human mast cells. Tryptase has been implicated in a variety of biological processes, including degradation of vasodilating and bronchorelaxing neuropeptides (Caughey, et al., J. Pharmacol. Exp. Ther., 1988, 244, pages 133-137; Franconi, et al., J. Pharmacol. Exp. Ther., 1988, 248, pages 947-951; and Tam, et al., Am. J. Respir. Cell Mol. Biol., 1990, 3, pages 27-32) and modulation of bronchial responsiveness to histamine (Sekizawa, et al., J. Clin. Invest., 1989, 83, pages 175-179). As a result, tryptase inhibitors may be useful as anti-inflammatory agents (K Rice, P.A. Sprengler, Current Opinion in Drug Discovery and Development, 1999, 2(5), pages 463-474) particularly in the treatment of chronic asthma (M.Q. Zhang, H. Timmerman, Mediators Inflamm., 1997, 112, pages 311-317) and may also be useful in treating or preventing allergic rhinitis (S. J. Wilson et al, Clin. Exp. Allergy, 1998, 28, pages 220-227), inflammatory bowel disease (S.C. Bischoff et al, Histopathology, 1996, 28, pages 1-13), psoriasis (A. Naukkarinen et al, Arch. Dermatol. Res., 1993, 285, pages 341-346), conjunctivitis (A.A.Irani et al, J. Allergy Clin. Immunol., 1990, 86, pages 34-40), atopic dermatitis (A. Jarvikallio et al, Br. J. Dermatol., 1997, 136, pages 871-877), rheumatoid arthritis (L.C Tetlow et al, Ann. Rheum. Dis., 1998, 54, pages 549-555), osteoarthritis (M.G. Buckley et al, J. Pathol., 1998, 186, pages 67-74), gouty arthritis, rheumatoid spondylitis, and diseases of joint cartilage destruction.

In addition, tryptase has been shown to be a potent mitogen for fibroblasts, suggesting its involvement in the pulmonary fibrosis in asthma and interstitial lung diseases (Ruoss et al., J. Clin. Invest., 1991, 88, pages 493-499). Therefore, tryptase inhibitors may be useful in treating or preventing fibrotic conditions (J.A. Cairns and A.F. Walls, J. Clin. Invest., 1997, 99, pages 1313-1321) for example,

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fibrosis, sceleroderma, pulmonary fibrosis, liver cirrhosis, myocardial fibrosis, neurofibromas and hypertrophic scars.

Additionally, tryptase inhibitors may be useful in treating or preventing myocardial infarction, stroke, angina and other consequences of atherosclerotic plaque rupture (M. Jeziorska et al, J. Pathol., 1997, 182, pages 115-122). Tryptase has also been discovered to activate prostromelysin that in turn activates collagenase, thereby initiating the destruction of cartilage and periodontal connective tissue, respectively. Therefore, tryptase inhibitors could be useful in the treatment or prevention of arthritis, periodontal disease, diabetic retinopathy, and tumor growth (W.J. Beil et al, Exp. Hematol., (1998) 26, pages 158-169). Also, tryptase inhibitors may be useful in the treatment of anaphylaxis (L.B. Schwarz et al, J. Clin. Invest., 1995, 96, pages 2702-2710), multiple sclerosis (M. Steinhoff et al, Nat. Med. (N. Y.), 2000, 6(2), pages 151-158), peptic ulcers and syncytial viral infections.

Mast cell mediated inflammatory conditions, in particular asthma, are a growing public health concern. Asthma is frequently characterized by progressive development of hyper-responsiveness of the trachea and bronchi to both immunospecific allergens and generalized chemical or physical stimuli, which lead to the onset of chronic inflammation. Leukocytes containing IgE receptors, notably mast cells and basophils, are present in the epithelium and underlying smooth muscle tissues of bronchi. These leukocytes initially become activated by binding of specific inhaled antigens to the IgE receptors and then release a number of chemical mediators. For example, degranulation of mast cells leads to the release of proteoglycans, peroxidase, arylsulfatase B, tryptase and chymase, which results in bronchiole constriction.

Accordingly, what is needed is a novel and useful group of compounds having valuable pharmaceutical properties, particularly, the ability to inhibit tryptase. Such compounds readily have utility in treating a patient suffering condition that can be ameliorated by the administration of an inhibitor of tryptase, e.g., mast cell mediated inflammatory conditions, inflammation, and diseases or disorders related to the degradation of vasodilating and bronchorelaxing neuropeptides. Particular examples of such conditions are described *infra*.

The citation of any reference herein should not be construed as an admission that such reference is available as "Prior Art" to the instant application.

SUMMARYOF THE INVETNION

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Broadly, the present invention extends to a compound of formula (I):-

$$R^{3}$$
 C
 O
 R^{4}
 CH_{2}
 D
 A
 R^{1}
 R^{2}
 R^{2}
 (I)

 $R^{\frac{1}{2}}$ NH_2

such that Ar is an aryl group or a heteroaryl group, and the

group is beta to the

wherein:-

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is a single or a double bond;

R¹ and R² are each independently hydrogen or lower alkyl;

R³ is aryl, arylalkenyl, cycloalkenyl, cycloalkyl, heteroaryl, heteroarylalkenyl, heterocycloalkenyl, a carbon linked heterocycloalkyl or alkyl optionally substituted by one or more groups selected from hydroxy, alkyloxycarbonylamino, cycloalkyl, heterocycloalkyl, R⁶, -OR⁶, -S(O)_mR⁶ or -C(=O)-R⁶;

 R^4 is hydrogen, acyl, alkoxy, alkyloxycarbonyl, carboxy, cyano, halo, hydroxy, $-C(=0)-NY^1Y^2$ or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, hydroxy,

15 $-S(O)_m$ -alkyl or -NY¹Y²;

 R^5 is hydrogen, acyl, alkoxy, alkyloxycarbonyl, aryl, carboxy, cyano, halo, heteroaryl, heteroaryloxy, heterocycloalkyl, heterocycloalkyloxy, heterocycloalkyloxy, heteroarylalkyloxy, hydroxy, trifluoromethyl, $-C(=O)-NY^1Y^2$, $-NY^1Y^2$, $-Z^1-C_{2-6}$ alkylene- R^7 or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, aryl, heteroaryl, heterocycloalkyl, hydroxy, ureido, $-C(=O)-NY^1Y^2$, $-SO_2-NY^1Y^2$, $-S(O)_m$ -alkyl or $-NY^1Y^2$;

R⁶ is aryl or heteroaryl;

 R^7 is hydroxy, alkoxy, ureido, $-C(=O)-NY^1Y^2$, $-SO_2-NY^1Y^2$, $-S(O)_m$ -alkyl or $-NY^1Y^2$; R^8 is hydrogen or lower alkyl;

 Y^1 and Y^2 are independently hydrogen, alkenyl, alkyl, aryl, arylalkyl, cycloalkyl, heteroaryl, heteroarylalkyl or heterocycloalkyl; or the group -NY 1 Y 2 may form a cyclic amine;

 Z^1 is O, S(O)_m or NR⁸;

m is zero or an integer 1 to 2;

- 5 n is zero or an integer 1 to 4;
 - an N-oxide of said compound, a prodrug of said compound, a pharmaceutically acceptable salt of said compound, a solvate of said compound, and a hydrate of said compound.
- Furthermore, the present invention extends to a compound of formula (Ia): -

wherein:-

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is a single or a double bond;

 R^1 and R^2 are each independently hydrogen or lower alkyl;

 R^3 is aryl, arylalkenyl, cycloalkenyl, cycloalkyl, heteroaryl, heteroarylalkenyl, heterocycloalkenyl, a carbon linked heterocycloalkyl or alkyl optionally substituted by one or more groups selected from hydroxy, alkoxy, alkyloxycarbonylamino, cycloalkyl, heterocycloalkyl, R^6 , $-OR^6$, $-S(O)_mR^6$ or

 $-C(=O)-R^{6}$;

R⁴ is hydrogen, acyl, alkoxy, alkyloxycarbonyl, carboxy, cyano, halo, hydroxy, -C(=O)-NY¹Y² or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, hydroxy, -S(O)_m-alkyl or -NY¹Y²;

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 R^5 is hydrogen, acyl, alkoxy, alkyloxycarbonyl, aryl, carboxy, cyano, halo, heteroaryl, heteroaryloxy, heterocycloalkyl, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroarylalkyloxy, hydroxy, trifluoromethyl, $-C(=O)-NY^1Y^2$, $-NY^1Y^2$, $-Z^1-C_{2-6}$ alkylene- R^7 or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, aryl, heteroaryl, heterocycloalkyl, hydroxy, ureido, $-C(=O)-NY^1Y^2$, $-SO_2-NY^1Y^2$, $-S(O)_m$ -alkyl or $-NY^1Y^2$;

R⁶ is aryl or heteroaryl;

R⁷ is hydroxy, alkoxy, ureido, -C(=O)-NY¹Y², -SO₂-NY¹Y², -S(O)_m-alkyl or -NY¹Y²;

R⁸ is hydrogen or lower alkyl;

 Y^1 and Y^2 are independently hydrogen, alkenyl, alkyl, aryl, arylalkyl, cycloalkyl, heteroaryl,

heteroarylalkyl or heterocycloalkyl; or the group -NY 1Y2 may form a cyclic amine;

 Z^1 is O, S(O)_m or NR⁸;

m is zero or an integer 1 to 2;

n is zero or an integer 1 to 4;

and the corresponding N-oxides, and their prodrugs; and pharmaceutically acceptable salts and solvates (e.g. hydrates) of such compounds and their N-oxides and prodrugs.

2. In another embodiment, the present invention extends to a compound of formula (Ib):

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 R^3 is aryl, arylalkenyl, cycloalkenyl, cycloalkyl, heteroaryl, heteroarylalkenyl, heterocycloalkenyl, a carbon linked heterocycloalkyl or alkyl optionally substituted by one or more groups selected from hydroxy, alkoxy, alkyloxycarbonylamino, cycloalkyl, heterocycloalkyl, R^6 , $-OR^6$, $-S(O)_mR^6$ or

25 $-C(=0)-R^6$:

 R^4 is hydrogen, acyl, alkoxy, alkyloxycarbonyl, carboxy, cyano, halo, hydroxy, $-C(=O)-NY^1Y^2$ or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, hydroxy, $-S(O)_m$ -alkyl or $-NY^1Y^2$; and

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 R^5 is hydrogen, acyl, alkoxy, alkyloxycarbonyl, aryl, carboxy, cyano, halo, heteroaryl, heteroaryloxy, heterocycloalkyl, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroarylalkyloxy, hydroxy, trifluoromethyl, $-C(=O)-NY^1Y^2$, $-NY^1Y^2$, $-Z^1-C_2$ -6alkylene- R^7 or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, aryl, heteroaryl, heterocycloalkyl, hydroxy, ureido, $-C(=O)-NY^1Y^2$, $-SO_2-NY^1Y^2$, $-S(O)_m$ -alkyl or $-NY^1Y^2$, and, a corresponding N-oxide of said compound, a prodrug of said compound, a pharmaceutically acceptable salt of said compound, a solvate of said compound, an N-oxides and prodrugs.

Particular examples of such compounds are described infra.

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Furthermore, the present invention extends to a pharmaceutical composition comprising a compound of the present invention, as described above, and a pharmaceutically acceptable carrier thereof. Numerous examples of pharmaceutical carriers having applications in the present invention are described *infra*.

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In addition, the present invention extends to a method for treating a patient suffering from a condition that can be ameliorated by the administration of an inhibitor of tryptase, comprising administering an effective amount of a compound of a compound of the present invention. An example of a condition that can be treated with a compound of the present invention includes, but certainly is not limited to inflammatory diseases, e.g., joint inflammation, arthritis, rheumatoid arthritis, rheumatoid spondylitis, gouty arthritis, traumatic arthritis, rubella arthritis, psoriatic arthritis, and other chronic inflammatory joint diseases. Other examples of conditions that can be treated with a method of the present invention include diseases of joint cartilage destruction, ocular conjunctivitis, vernal conjunctivitis, inflammatory bowel disease, asthma, allergic rhinitis, interstitial lung diseases, fibrosis, sceleroderma, pulmonary fibrosis, liver cirrhosis, myocardial fibrosis, neurofibromas, hypertrophic scars, various dermatological conditions, for example, atopic dermatitis and psoriasis, myocardial infarction, stroke, angina and other consequences of atherosclerotic plaque rupture, as well as periodontal disease, diabetic retinopathy, tumor growth, anaphylaxis, multiple sclerosis, peptic ulcers, and syncytial viral infections, to name only a few.

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In a particular embodiment, the present invention extends to a method of treating a subject suffering from asthma, comprising administering to the subject an effective amount of a compound of the present invention.

In another embodiment, the present invention extends to a method for treating a patient suffering from joint inflammation, comprising administering to the patient an effective amount of a compound of the present invention.

In addition, the present invention extends to a pharmaceutical comprising a compound of the present invention, a second compound selected from the group consisting of a beta andrenergic agonist, an anticholinergic, an anti-inflammatory corticosteroid, and an anti-inflammatory agent, and a pharmaceutically acceptable carrier thereof. Particular inflammatory diseases or disorders that can be treated with such a pharmaceutical composition includes, but certainly is not limited to asthma.

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Moreover, the present invention extends to a method for treating a patient suffering from an inflammatory disorder, comprising administering to the patient a compound of the present invention and a second compound selected from the group consisting of a beta andrenergic agonist, an anticholinergic, an anti-inflammatory corticosteroid, and an anti-inflammatory agent. In such a method of the present invention, a compound of the present invention can be administered to the patient before a second compound, a second compound can be administered to the patient before a compound of the present invention, or a compound of the present invention and a second compound can be administered concurrently. Particular examples of andrenergic agonists, anticholinergics, anti-inflammatory corticosteroids, and anti-inflammatory agents having applications in a method of the present invention are described *infra*.

Accordingly, it is a principal object to provide compounds having an anti-tryptase activity. Such compounds can readily be used to treat a condition that can be ameliorated by the administration of an inhibitor of tryptase.

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It is another object of the present invention to provide pharmaceutical compositions for treating a condition that can be ameliorated by the administration of an inhibitor of tryptase.

It is yet another object of the present invention to provide pharmaceutical compositions comprising a compound of the present invention.

These and other aspects of the present invention will be better appreciated by reference to the following Detailed Description.

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DETAILED DESCRIPTION

As used above, and throughout the instant specification and appending claims, the following terms, unless otherwise indicated, shall be understood to have the following meanings:-

As used herein, the term "compounds of the present invention", and equivalent expressions, are meant to embrace compounds of formulae (I), (Ia), or (Ib) as hereinbefore described, which expression includes the prodrugs, the pharmaceutically acceptable salts and the solvates, e.g. hydrates, where the context so permits. Similarly, reference to intermediates, whether or not they themselves are claimed, is meant to embrace their salts, and solvates, where the context so permits. For the sake of clarity, particular instances when the context so permits are sometimes indicated in the text, but these instances are purely illustrative and it is not intended to exclude other instances when the context so permits.

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As used herein, the term "treatment" includes prophylactic therapy as well as treatment of an established condition.

"Patient" includes both human and other mammals.

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"Effective amount" is meant to describe an amount of compound of the present invention effective in inhibiting tryptase and thus producing the desired therapeutic effect.

"Acyl" means an H-CO- or alkyl-CO- group in which the alkyl group is as described herein.

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"Acylamino" is an acyl-NH- group wherein acyl is as defined herein.

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"Alkenyl" means an aliphatic hydrocarbon group containing a carbon-carbon double bond and which may be straight or branched having about 2 to about 15 carbon atoms in the chain. Preferred alkenyl groups have 2 to about 12 carbon atoms in the chain; and more preferably about 2 to about 4 carbon atoms in the chain. "Branched", as used herein and throughout the text, means that one or more lower alkyl groups such as methyl, ethyl or propyl are attached to a linear chain; here a linear alkenyl chain. "Lower alkenyl" means about 2 to about 4 carbon atoms in the chain that may be straight or branched. Exemplary alkenyl groups include ethenyl, propenyl, n-butenyl, i-butenyl, 3-methylbut-2-enyl, n-pentenyl, heptenyl, octenyl and decenyl.

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"Alkoxy" means an alkyl-O- group in which the alkyl group is as described herein. Exemplary alkoxy groups include methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy and heptoxy.

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"Alkyloxycarbonyl" means an alkyl-O-C(=O)- group in which the alkyl group is as described herein. Exemplary alkyloxycarbonyl groups include methoxy- and ethoxycarbonyl.

"Alkyl" means, unless otherwise specified, an aliphatic hydrocarbon group which may be straight or branched having about 1 to about 15 carbon atoms in the chain optionally substituted by alkoxy or by one or more halogen atoms. Particular alkyl groups have from 1 to about 6 carbon atoms. "Lower alkyl" as a group or part of a lower alkoxy, lower alkylthio, lower alkylsulfinyl or lower alkylsulfonyl group means unless otherwise specified, an aliphatic hydrocarbon group which may be straight or branched having about 1 to about 4 carbon atoms in the chain. Exemplary alkyl groups include methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, 3-pentyl, heptyl, octyl, nonyl, decyl and dodecyl.

"Alkylcarbonylamino" means an alkyl-C(=O)-NH- group in which the alkyl group is as described herein. Exemplary alkylcarbonylamino groups include acetamido and propionamido.

"Alkylene" means an aliphatic bivalent radical derived from a straight or branched alkyl group, in which the alkyl group is as described herein. Exemplary alkylene radicals include methylene, ethylene and trimethylene.

"Alkylenedioxy" means an -O-alkyl-O- group in which the alkyl group is as defined above. Exemplary alkylenedioxy groups include methylenedioxy and ethylenedioxy.

"Alkylsulfinyl" means an alkyl-SO- group in which the alkyl group is as previously described.

Preferred alkylsulfinyl groups are those in which the alkyl group is C₁₋₄alkyl.

"Alkylsulfonyl" means an alkyl-SO₂- group in which the alkyl group is as previously described. Preferred alkylsulfonyl groups are those in which the alkyl group is C₁₋₄alkyl.

"Alkylsulfonylamino" means an alkyl-SO₂-NH- group in which the alkyl group is as described herein. Exemplary alkylsulfonylamino groups include methanesulfonamido and ethanesulfonamido.

"Alkylthio" means an alkyl-S- group in which the alkyl group is as previously described. Exemplary alkylthio groups include methylthio, ethylthio, isopropylthio and heptylthio.

"Alkynyl" means an aliphatic hydrocarbon group containing a carbon-carbon triple bond and which may be straight or branched having about 2 to about 15 carbon atoms in the chain. Preferred alkynyl groups have 2 to about 12 carbon atoms in the chain; and more preferably about 2 to about 4 carbon atoms in the chain. Exemplary alkynyl groups include ethynyl, propynyl, n-butynyl, 2-butynyl, 3-methylbut-2-ynyl, and n-pentynyl.

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"Aroyl" means an aryl-CO- group in which the aryl group is as described herein. Exemplary aroyl groups include benzoyl and 1- and 2-naphthoyl.

5 "Aroylamino" is an aroyl-NH- group wherein aroyl is as previously defined.

"Aryl" as a group or part of a group denotes: (i) an optionally substituted monocyclic or multicyclic aromatic carbocyclic moiety of about 6 to about 14 carbon atoms, such as phenyl or naphthyl; or (ii) an optionally substituted partially saturated multicyclic aromatic carbocyclic moiety in which an aryl and a cycloalkyl or cycloalkenyl group are fused together to form a cyclic structure, such as a tetrahydronaphthyl, indenyl or indanyl ring. Aryl groups may be substituted with one or more aryl group substituents which may be the same or different, where "aryl group substituent" includes, for example, acyl, acylamino, alkoxy, alkyloxycarbonyl, alkylenedioxy, alkylsulfinyl, alkylsulfonyl, alkylthio, aroyl, aroylamino, aryl, arylalkenyl, arylalkynyl, arylalkyloxy, arylalkyloxycarbonyl, arylalkylthio, aryloxy, aryloxyalkyl, aryloxycarbonyl, arylsulfinyl, arylsulfonyl, arylthio, carboxy, cyano, halo, heteroaryloxy, heteroarylalkenyl, heteroarylalkynyl, heteroarylalkyloxy, heteroarylalkyloxy, heteroarylalkyloxy, nitro, trifluoromethyl, -NY¹Y², -CONY¹Y², -SO₂NY¹Y², -Z²-C₂-6alkylene-NY¹Y² {where Z² is O, NR⁸ or S(O)_m}, -NY¹-(C=O)alkyl, -NY¹-SO₂alkyl or alkyl optionally substituted with alkoxy, aroyl, aryl, aryloxy, heteroaryl, hydroxy, or -NY¹Y².

"Arylalkenyl" means an aryl-alkenyl- group in which the aryl and alkenyl are as previously described. Preferred arylalkenyls contain a lower alkenyl moiety. Exemplary arylalkenyl groups include styryl and phenylallyl.

"Arylalkyl" means an aryl-alkyl- group in which the aryl and alkyl moieties are as previously described. Preferred arylalkyl groups contain a C_{1-4} alkyl moiety. Exemplary arylalkyl groups include benzyl, 2-phenethyl and naphthlenemethyl.

"Arylalkyloxy" means an arylalkyl-O- group in which the arylalkyl groups is as previously described.

Exemplary arylalkyloxy groups include benzyloxy and 1- or 2-naphthalenemethoxy.

"Arylalkyloxycarbonyl" means an arylalkyl-O-CO- group in which the arylalkyl groups is as previously described. An exemplary arylalkyloxycarbonyl group is benzyloxycarbonyl.

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- "Arylalkylthio" means an arylalkyl-S- group in which the arylalkyl group is as previously described. An exemplary arylalkylthio group is benzylthio.
- "Arylalkynyl" means an aryl-alkynyl- group in which the aryl and alkynyl are as previously described. Exemplary arylalkynyl groups include phenylethynyl and 3-phenylbut-2-ynyl.
 - "Aryloxy" means an aryl-O- group in which the aryl group is as previously described. Exemplary aryloxy groups include optionally substituted phenoxy and naphthoxy.
- "Aryloxyalkyl" means an aryl-O-alkyl- group in which the aryl and alkyl groups are as previously described. Exemplary aryloxyalkyl groups include phenoxymethyl and 1- or 2-naphthyloxymethyl.
 - "Aryloxycarbonyl" means an aryl-O-C(=O)- group in which the aryl group is as previously described. Exemplary aryloxycarbonyl groups include phenoxycarbonyl and naphthoxycarbonyl.
 - "Arylsulfinyl" means an aryl-SO- group in which the aryl group is as previously described.
 - "Arylsulfonyl" means an aryl-SO₂- group in which the aryl group is as previously described.
- 20 "Arylthio" means an aryl-S- group in which the aryl group is as previously described. Exemplary arylthio groups include phenylthio and naphthylthio.
 - "Azaheteroaryl" means an aromatic carbocyclic moiety of about 5 to about 10 ring members in which one of the ring members is nitrogen and the other ring members are chosen from carbon, oxygen, sulfur, or nitrogen. Examples of azaheteroaryl groups include benzimidazolyl, imidazolyl, isoquinolinyl, isoxazolyl, pyrazolopyrimidinyl, pyridyl, pyrimidinyl, quinolinyl, quinazolinyl and thiazolyl.
 - "Cyclic amine" means a 3 to 8 membered monocyclic cycloalkyl ring system where one of the ring carbon atoms is replaced by nitrogen and which (i) may optionally contain an additional heteroatom selected from O, S or NY³ (where Y³ is hydrogen, alkyl, arylalkyl, and aryl) and (ii) may be fused to additional aryl or heteroaryl ring to form a bicyclic ring system. Exemplary cyclic amines include pyrrolidine, piperidine, morpholine, piperazine, indoline and pyrindoline.
- "Cycloalkenyl" means a cycloalkyl group containing at least one carbon-carbon double bond.

 Exemplary monocyclic cycloalkenyl rings include cyclopentenyl, cyclohexenyl or cycloheptenyl.

"Cycloalkyl" means a saturated monocyclic or bicyclic ring system of about 3 to about 10 carbon atoms optionally substituted by oxo, alkyl, aryl or -C(=O)- NY¹Y². Exemplary monocyclic cycloalkyl rings include C₃₋₈cycloalkyl rings such as cyclopropyl, cyclopentyl, cyclohexyl and cycloheptyl.

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"Cycloalkylalkyl" means a cycloalkyl-alkyl- group in which the cycloalkyl and alkyl moieties are as previously described. Exemplary monocyclic cycloalkylalkyl groups include cyclopropylmethyl, cyclopentylmethyl, cyclohexylmethyl and cycloheptylmethyl.

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"Halo" or "halogen" means fluoro, chloro, bromo, or iodo. Preferred are fluoro or chloro.

"Heteroaroyl" means a heteroaryl-C(=O)- group in which the heteroaryl group is as described herein. Exemplary groups include pyridylcarbonyl.

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"Heteroaroylamino" means a heteroaroyl-NH- group in which the heteroaryl mojety are as previously described.

"Heteroary!" as a group or part of a group denotes: (i) an optionally substituted aromatic monocyclic or

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multicyclic organic moiety of about 5 to about 10 ring members in which one or more of the ring members is/are element(s) other than carbon, for example nitrogen, oxygen or sulfur (examples of such groups include benzimidazolyl, benzthiazolyl, benzthiophenyl, furyl, imidazolyl, indolyl, indolyl, indolyl, isoxazolyl, isoquinolinyl, isothiazolyl, oxadiazolyl, pyrazinyl, pyridazinyl, pyrazolyl, pyridyl, pyrimidinyl, pyrrolyl, quinazolinyl, quinolinyl, 1,3,4-thiadiazolyl, thiazolyl, thienyl and triazolyl groups, optionally substituted by one or more aryl group substituents as defined above); (ii) an optionally substituted partially saturated multicyclic heterocarbocyclic moiety in which a heteroaryl and a cycloalkyl or cycloalkenyl group are fused together to form a cyclic structure (examples of such

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groups include pyrindanyl groups). Optional substituents include one or more "aryl group substituents" as defined above.

Substitu

"Aryldiyl" means an optionally substituted bivalent radical derived from an aryl group as defined herein. Exemplary aryldiyl groups include optionally substituted phenylene, naphthylene and indanylene. Suitable substituents include one or more "aryl group substituents" as defined above, particularly halogen, methyl or methoxy.

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"Heteroaryldiyl" means a bivalent radical derived from a heteroaryl group as defined below.

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"Heteroarylalkenyl" means a heteroaryl-alkenyl- group in which the heteroaryl and alkenyl moieties are as previously described. Preferred heteroarylalkenyl groups contain a lower alkenyl moiety. Exemplary heteroarylalkenyl groups include pyridylethenyl and pyridylallyl.

"Heteroarylalkyl" means a heteroaryl-alkyl- group in which the heteroaryl and alkyl moieties are as previously described. Preferred heteroarylalkyl groups contain a C₁₋₄alkyl moiety. Exemplary heteroarylalkyl groups include pyridylmethyl.

"Heteroarylalkyloxy" means an heteroarylalkyl-O- group in which the heteroarylalkyl group is as previously described. Exemplary heteroaryloxy groups include optionally substituted pyridylmethoxy.

"Heteroarylalkynyl" means a heteroaryl-alkynyl- group in which the heteroaryl and alkynyl moieties are as previously described. Exemplary heteroarylalkenyl groups include pyridylethynyl and 3-pyridylbut-2-ynyl.

"Heteroaryloxy" means an heteroaryl-O- group in which the heteroaryl group is as previously described. Exemplary heteroaryloxy groups include optionally substituted pyridyloxy.

"Heteroaryloxyalkyl" means an heteroaryl-O-alkyl- group in which the heteroaryl and alkyl groups are as previously described. Exemplary heteroaryloxyalkyl groups include pyridyoxymethyl and 2-, 3- or 4-quinolinyloxymethyl.

"Heterocycloalkenyl" means a cycloalkenyl group of about 3 to 7 ring members which contains one or more heteroatoms selected from O, S or NY⁴ (where Y⁴ is hydrogen, alkyl, aryl, arylalkyl, and alkyloxycarbonyl). Exemplary heterocycloalkenyl groups include 1,2,3,6-tetrahydro-pyridine.

"Heterocycloalkyl" means: (i) a cycloalkyl group of about 3 to 7 ring members which contains one or more heteroatoms selected from O, S or NY⁴ (where Y⁴ is hydrogen, alkyl, aryl, arylalkyl, and alkyloxycarbonyl) and which may optionally be substituted by oxo (examples of such groups include piperidinyl, pyrrolidinyl, morpholinyl, tetrahydropyranyl and tetrahydrothiophenyl; (ii) an optionally substituted partially saturated multicyclic heterocarbocyclic moiety in which one or more aryl (or heteroaryl) rings and a cycloalkyl group of about 3 to 7 ring members, which contains one or more heteroatoms selected from O, S or NY⁴ and which may optionally be substituted by oxo, are fused together to form a cyclic structure (examples of such groups include chromanyl, dihydrobenzofuranyl, indolinyl and pyrindolinyl groups).

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"Heterocycloalkylalkyl" means a heterocycloalkyl-alkyl- group in which the heterocycloalkyl and alkyl moieties are as previously described.

"Heterocycloalkylalkyloxy" means a heterocycloalkyl-alkyl-O- group in which the heterocycloalkyl and alkyl moieties are as previously described.

"Heterocycloalkyloxy" means a heterocycloalkyl-O- group in which the heterocycloalkyl is as previously described.

"Prodrug" means a compound which is suitable for administration to a patient without undue toxicity, irritation, allergic response, and the like, and is convertible in vivo by metabolic means (e.g. by hydrolysis) to a compound of the present invention, including N-oxides thereof. A thorough discussion is provided in T. Higuchi and V. Stella, Pro-drugs as Novel Delivery Systems, Vol. 14 of the A. C. S. Symposium Series, and in Edward B. Roche, ed., Bioreversible Carriers in Drug Design,
 American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated herein by reference. For example an ester of a compound of the present invention containing a hydroxy group may be convertible by hydrolysis in vivo to the parent molecule. Alternatively an ester of a compound of the present invention containing a carboxy group may be convertible by hydrolysis in vivo to the parent molecule.

Suitable esters of compounds of present invention containing a hydroxy group, are for example acetates, citrates, lactates, tartrates, malonates, oxalates, salicylates, propionates, succinates, fumarates, maleates, methylene-bis-β-hydroxynaphthoates, gentisates, isethionates, di-p-toluoyltartrates, methanesulfonates, ethanesulfonates, benzenesulfonates, p-toluenesulfonates, cyclohexylsulfamates and quinates.

An especially useful class of esters of compounds of the present invention containing a hydroxy group, may be formed from acid moieties selected from those described by Bundgaard et al., J. Med. Chem., 1989, 32, page 2503-2507, and include substituted (aminomethyl)-benzoates, for example dialkylamino-methylbenzoates in which the two alkyl groups may be joined together and/or interrupted by an oxygen atom or by an optionally substituted nitrogen atom, e.g. an alkylated nitrogen atom, more especially (morpholino-methyl)benzoates, e.g. 3- or 4-(morpholinomethyl)-benzoates, and (4-alkylpiperazin-1-yl)benzoates, e.g. 3- or 4-(4-alkylpiperazin-1-yl)benzoates.

Suitable esters of compounds of the present invention containing a carboxy group, are for example those described by F.J.Leinweber, Drug Metab. Res., 1987, 18, page 379.

The compounds of the present invention are basic, and such compounds are useful in the form of the free base or in the form of a pharmaceutically acceptable acid addition salt thereof.

Acid addition salts are a more convenient form for use; and in practice, use of the salt form inherently amounts to use of the free base form. The acids which can be used to prepare the acid addition salts include preferably those which produce, when combined with the free base, pharmaceutically acceptable salts, that is, salts whose anions are non-toxic to the patient in pharmaceutical doses of the salts, so that the beneficial inhibitory effects inherent in the free base are not vitiated by side effects ascribable to the anions. Although pharmaceutically acceptable salts of said basic compounds are preferred, all acid addition salts are useful as sources of the free base form even if the particular salt, per se, is desired only as an intermediate product as, for example, when the salt is formed only for purposes of purification, and identification, or when it is used as intermediate in preparing a pharmaceutically acceptable salt by ion exchange procedures. Pharmaceutically acceptable salts within the scope of the invention include those derived from mineral acids and organic acids, and include hydrohalides, e.g. hydrochlorides and hydrobromides, sulfates, phosphates, nitrates, sulfamates, acetates, citrates, lactates, tartrates, malonates, oxalates, salicylates, propionates, succinates, fumarates, maleates, methylene-bis-b-hydroxynaphthoates, gentisates, isethionates, di-p-toluoyltartrates, methane-sulfonates, ethanesulfonates, benzenesulfonates, p-toluenesulfonates, cyclohexylsulfamates and quinates.

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As well as being useful in themselves as active compounds, salts of compounds of the invention are useful for the purposes of purification of the compounds, for example by exploitation of the solubility differences between the salts and the parent compounds, side products and/or starting materials by techniques well known to those skilled in the art.

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With reference to formula (Ia) above, the following are particular and preferred groupings:

R¹ may particularly represent hydrogen.

30 R² may particularly represent hydrogen.

R³ may particularly represent aryl, such as optionally substituted phenyl or optionally substituted naphthyl, especially substituted phenyl. Exemplary optional substituents include one or more halo atoms or alkyl substituted by aryl, alkyl substituted by aryloxy, alkyl substituted by aroyl, alkyl substituted by heteroaryl, arylalkynyl, heteroarylalkynyl, aryl, heteroaryl, arylalkenyl or arylalkyloxy,

in which the aryl or heteroaryl groups may be further substituted by one or more aryl group substituents.

R³ may also particularly represent heteroaryl, such as optionally substituted pyridyl, optionally substituted quinolinyl, optionally substituted thienyl, optionally substituted furanyl or optionally substituted indolyl, especially substituted thienyl, substituted pyridyl or indolyl. Exemplary optional substitutents include alkyl substituted by aryl, alkyl substituted by aryloxy, alkyl substituted by aroyl, alkyl substituted heteroaryl, arylalkynyl, heteroarylalkynyl, heteroaryl, arylalkenyl or arylalkyloxy, in which the aryl or heteroaryl groups are further substituted by one or more aryl group substituents.

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R⁴ may particularly represent hydrogen.

R⁴ may also particularly represent cyano, especially when attached to the tertiary ring carbon atom.

15 R⁵ may particularly represent hydrogen.

R⁵ may also particularly represent lower alkyl (e.g. methyl) or halo (e.g. fluoro).

may particularly represent a single bond.

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n may particularly represent 2.

It is to be understood that this invention covers all appropriate combinations of the particular and preferred groupings referred to herein.

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A particular group of compounds of the invention are compounds of formula (Ib):-

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in which R³, R⁴ and R⁵ are as hereinbefore defined and the corresponding N-oxides, and their prodrugs; and pharmaceutically acceptable salts and solvates (e.g. hydrates) of such compounds and their N-oxides and prodrugs.

Compounds of formula (Ib) in which R³ represents aryl, such as optionally substituted phenyl or optionally substituted naphthyl, especially substituted phenyl, are preferred. Preferred optional substituents include one or more halo atoms or alkyl substituted by aryl or alkyl substituted heteroaryl, in which the aryl or heteroaryl groups may be further substituted by one or more aryl group substituents. R³ especially represents dichlorophenyl [e.g. 3,4-dichlorophenyl], phenylC₁₋₃alkylphenyl [e.g. phenethyl], hydroxyphenylC₁₋₃alkylphenyl [e.g. 4-hydroxyphenylchylphenyl] and aminopyridylC₁₋₃alkylphenyl [e.g. (4-amino-pyrid-3-yl)ethylphenyl].

Compounds of formula (Ib) in which R³ represents heteroaryl, such as optionally substituted pyridyl, optionally substituted quinolinyl, optionally substituted thienyl, optionally substituted furanyl or optionally substituted indolyl, especially substituted thienyl, substituted pyridyl or indolyl, are preferred. Preferred optional substituents include alkyl substituted by aryl and alkyl substituted heteroaryl in which the aryl or heteroaryl groups are further substituted by one or more aryl group substituents. R³ especially represents phenylC₁₋₃alkylpyridyl [e.g. 5-phenylethyl-pyrid-3-yl], phenylC₁₋₃alkylthienyl [e.g. 5-phenylethyl-thien-2-yl] and indolyl [e.g. indol-6-yl].

25 Compounds of formula (Ib) in which R⁴ represents hydrogen are preferred.

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Compounds of formula (Ib) in which R^4 represents cyano are also preferred. R^4 is preferably attached at the 4 position of the piperidine ring.

Compounds of formula (Ib) in which R⁵ represents hydrogen are preferred.

Compounds of formula (Ib) in which R⁵ represents lower alkyl (e.g. methyl) or halo (e.g. fluoro), are also preferred. R⁵ is preferably attached to the phenyl ring in the position para to the -CH₂NH₂ group.

A preferred group of compounds of the invention are compounds of formula (Ib) in which:- R³ is substituted phenyl [especially 3,4-dichlorophenyl, phenethyl, 4-hydroxyphenylethylphenyl and (4-amino-pyrid-3-yl)ethylphenyl] or optionally substituted heteroaryl [especially 5-phenylethyl-pyrid-3-yl, 5-phenylethyl-thien-2-yl or indol-6-yl]; R⁴ is hydrogen, or cyano attached at the 4 position of the piperidine ring; R⁵ is hydrogen, or lower alkyl (e.g. methyl) or halo (e.g. fluoro) attached to the phenyl ring in the position para to the -CH₂NH₂ group; and the corresponding N-oxides, and their prodrugs; and pharmaceutically acceptable salts and solvates (e.g. hydrates) of such compounds and their N-oxides and prodrugs.

Particular compounds of the invention are selected from the compounds formed by joining the carbon atom (C*) of one of the fragments (A1 to A10) shown in Table 1 to the carbon atom (C*) of one of the fragments (B1 to B12) shown in Table 2, and joining the nitrogen atom (N*) of one of the fragments (B1 to B12) shown in Table 2 to the carbon atom (C*) of one of the acidic fragments (C1 to C103) depicted in Table 3.

TABLE 1

A1	CH ₂ -NH ₂	A2	HOCH ₂ CH ₂ O Č CH ₂ -NH ₂
A3	CH ₂ -NH ₂	A4	CH ₃ OCH ₂ CH ₂ O CH ₂ -NH ₂

A 5	CH ₃ O CH ₂ -NH ₂	A6	HO CH ₂ -NH ₂
A7	H ₃ C Č CH ₂ -NH ₂	A8	CH ₂ -NH ₂
A9	F ₃ C CH ₂ -NH ₂	A10	H ₃ C CH ₂ O CCH ₂ -NH ₂
A11	H ₂ N S	A12	CH ₂ -NH ₂

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TABLE 2

B1	* N C *	B2	CH ³ O C C X
В3	HOCH ₂ C	В4	CH ₃ OCH ₂ C
В5	CH ₃ C (=0) -NH-CH ₂	В6	CH ₃ SO ₂ -NH-CH ₂ C
В7	ř K K	В8	NC *
В9	HO C *	B10	HO *
B11	HOCH ₂	B12	CH ₃ CH ₂ O C
B13	CH ₃ CH ₂ O C *		INTENTIONALLY LEFT BLANK

TABLE 3

C1	C1 C1	C2	C*
СЗ	H N O C *	C4	©=c*
C5	S C*	C6	HN C*
C7	HO C *	C8	0=c*
C9	O II c*	C10	s c*
C11	°=*	C12	H ₂ N O C*
C13		C14	

C15	°Ec*	C16	H ₂ N N C C C*
C17	N C*	C18	N O C*
C19	°*	C20	C C C C C C C C C C C C C C C C C C C
C21	°≡c*	C22	0=c*
C23	0 0 0 0 0 0 0 0	C24	HN C*
C25	0 	C26	H ₃ C

C27	il.*	C28	CH ₃ O C*
C29	°°c*	C30	NH OI C*
C31	0=c*	C32	0 c*
C33	0=*	C34	O CM
C35	°E*	C36	(CH ₃) ₃ C
C37	CH ₃	C38	(CH ₃) 3C-CH ₂ C*

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C39	0=c*	C40	CH ₃ O C*
C41	CH ₃ O O = C*	C42	CH ₃
C43	H ₃ C CH ₃ C* CH ₃ CH ₃	C44	CH ₃ O
C45	H ₃ C	C46	C1 CH ₃ CH ₃
C47	(CH ₃) 3C C*	C48	CH ₃ O C*
C49	CH ₃ O C*	C50	CF ₃ C*

C51	(CH ₃) ₂ N	C52	©=c*
C53	s s	C54	o≡c*
C55	C*	C56	SCH ₃
C57	c1 0 c*	C58	°C*
C59	(CH ₃) ₂ CH C*	C60	O C*
C61	N C*	C62	(CH ₃) ₃ C
C63	CH ₃	C64	on the second se

C65	O II C*	C66	
C67	CH ³ CC*	C68	° ° ° ° ° ° ° ° ° ° ° ° ° ° ° ° ° ° °
C69	Br C* OCH2CH3	C70	CH ₃ O C*
C71	CH ₃ (CH ₂) 3 C*	C72	CH ₃
C73	H ₃ C N C1	C74	C* (CH ₂) ₂ CH ₃

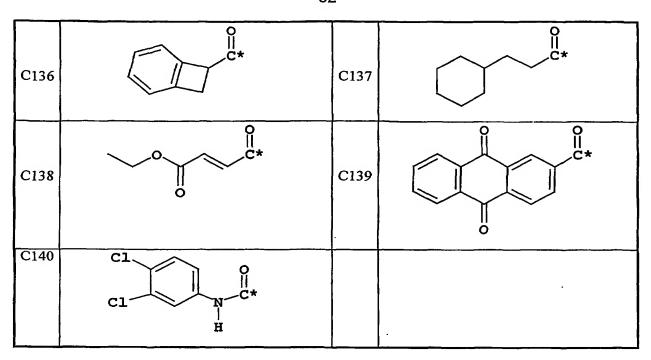
C75	C1 (CH ₂) ₂ CH ₃	C76	(CH ₃) ₂ N O
C77	C1 OH*	C78	0=c*
C79	O III c*	C80	H ₃ C C* CH ₃
C81	o = c	C82	CH ₃ S C*
C83	CF ₃ S C*	C84	0=c*

C85	o=c*	C86	H ₃ C C*
C87	CH ₃ CH ₂	C88	H ₃ C N CH ₃
C89	NH ₂ O II C*	C90	CH ₃ CH ₂ O O C*
C91	o≡¢*	C92	CH ₃ O O O CH ₃
C93	CH ₃ O C*	C94	H ₃ C O
C95	CH ₃ O O C*	C96	СH ₃ (СH ₂) 3 С*

C97	CH ₃ (CH ₂) 4 C*	C98	CH ₃ C*
C99	(CH ₃) 3C O H C*	C100	(CH ₃) ₃ C O N C*
C101	(CH ₃) ₃ C N C*	C102	(CH ³) ³ C
C103	°=*		INTENTIONALLY LEFT BLANK
C104	CH ₃ S C*	C105	s c*
C106	O C *	C107	© c c c c c c c c c
C108	F O C*	C109	C1 C*

C110	C1	C111	Ĉ*
C112	CH ₃ S C*	C113	H ₂ N O C*
C114	F 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	C115	O C*
C116	0 C*	C117	C1—S
C118	F Br	C119	I C*
C120	F C*	C121	C*

C122	C1 C* NH ₂	C123	0 - - - - - -
C124	ÖÜ*	C125	F C*
C126	0-N-C*	C127	OH OH
C128	°E*	C129	0 N 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
C130	°≡c*	C131	OCH ₃ O C*
C132	F O O C*	C133	HO CN
C134	HO C*	C135	S C*



Particularly preferred examples of fragments "A", "B", and "C" are illustrated in Table 4 below:

	TABLE 4					
5	A1-B1-C1	A1-B1-C2	A1-B1-C3	A1-B1-C4	A1-B1-C5	A1-B1-C6
	A1-B1-C7	A1-B1-C8	A1-B1-C9	A1-B1-C10	A1-B1-C11	A1-B1-C12
	A1-B1-C13	A1-B1-C14	A1-B1-C15	A1-B1-C16	A1-B1-C17	A1-B1-C18
	A1-B1-C19	A1-B1-C20	A1-B1-C21	A1-B1-C22	A1-B1-C23	A1-B1-C24
	A1-B1-C25	A1-B1-C26	A1-B1-C27	A1-B1-C28	A1-B1-C29	A1-B1-C30
10	A1-B1-C31	A1-B1-C32	A1-B1-C33	A1-B1-C34	A1-B1-C35	A1-B1-C36
	A1-B1-C37	A1-B1-C38	A1-B1-C39	A1-B1-C40	A1-B1-C41	A1-B1-C42
	A1-B1-C43	A1-B1-C44	A1-B1-C45	A1-B1-C46	A1-B1-C47	A1-B1-C48
	A1-B1-C49	A1-B1-C50	A1-B1-C51	A1-B1-C52	A1-B1-C53	A1-B1-C54
	A1-B1-C55	A1-B1-C56	A1-B1-C57	A1-B1-C58	A1-B1-C59	A1-B1-C60
15	A1-B1-C61	A1-B1-C62	A1-B1-C63	A1-B1-C64	A1-B1-C65	A1-B1-C66
	A1-B1-C67	A1-B1-C68	A1-B1-C69	A1-B1-C70	A1-B1-C71	A1-B1-C72
	A1-B1-C73	A1-B1-C74	A1-B1-C75	A1-B1-C76	A1-B1-C77	A1-B1-C78
	A1-B1-C79	A1-B1-C80	A1-B1-C81	A1-B1-C82	A1-B1-C83	A1-B1-C84
	A1-B1-C85	A1-B1-C86	A1-B1-C87	A1-B1-C88	A1-B1-C89	A1-B1-C90
20	A1-B1-C91	A1-B1-C92	A1-B1-C93	A1-B1-C94	A1-B1-C95	A1-B1-C96
	A1-B1-C97	A1-B1-C98	A1-B1-C99	A1-B1-C100	A1-B1-C101	A1-B1-c102
	A1-B1-C103	A1-B1-C104	A1-B1-C105	A1-B1-C106	A1-B1-C107	A1-B1-C108
	A1-B1-C109	A1-B1-C110	A1-B1-C111	A1-B1-C112	A1-B1-C113	A1-B1-C114

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	A1-B1-C115	A1-B1-C116	A1-B1-C117	A1-B1-C118	A1-B1-C119	A1-B1-C120
	A1-B1-C121	A1-B1-C122	A1-B1-C123	A1-B1-C124	A1-B1-C125	A1-B1-C126
	A1-B1-C127	A1-B1-C128	A1-B1-C129	A1-B1-C130	A1-B1-C131	A1-B1-C132
	A1-B1-C133	A1-B1-C134	A1-B1-C135	A1-B1-C136	A1-B1-C137	A1-B1-C138
5	A1-B1-C139	A1-B1-C140	BLANK	BLANK	BLANK	BLANK
	A1-B2-C1	A1-B2-C2	A1-B2-C3	A1-B2-C4	A1-B2-C5	A1-B2-C6
	A1-B2-C7	A1-B2-C8	A1-B2-C9	A1-B2-C10	A1-B2-C11	A1-B2-C12
	A1-B2-C13	A1-B2-C14	A1-B2-C15	A1-B2-C16	A1-B2-C17	A1-B2-C18
	A1-B2-C19	A1-B2-C20	A1-B2-C21	A1-B2-C22	A1-B2-C23	A1-B2-C24
10	A1-B2-C25	A1-B2-C26	A1-B2-C27	A1-B2-C28	A1-B2-C29	A1-B2-C30
	A1-B2-C31	A1-B2-C32	A1-B2-C33	A1-B2-C34	A1-B2-C35	A1-B2-C36
	A1-B2-C37	A1-B2-C38	A1-B2-C39	A1-B2-C40	A1-B2-C41	A1-B2-C42
	A1-B2-C43	A1-B2-C44	A1-B2-C45	A1-B2-C46	A1-B2-C47	A1-B2-C48
	A1-B2-C49	A1-B2-C50	A1-B2-C51	A1-B2-C52	A1-B2-C53	A1-B2-C54
15	A1-B2-C55	A1-B2-C56	A1-B2-C57	A1-B2-C58	A1-B2-C59	A1-B2-C60
	A1-B2-C61	A1-B2-C62	A1-B2-C63	A1-B2-C64	A1-B2-C65	A1-B2-C66
	A1-B2-C67	A1-B2-C68	A1-B2-C69	A1-B2-C70	A1-B2-C71	A1-B2-C72
	A1-B2-C73	A1-B2-C74	A1-B2-C75	A1-B2-C76	A1-B2-C77	A1-B2-C78
	A1-B2-C79	A1-B2-C80	A1-B2-C81	A1-B2-C82	A1-B2-C83	A1-B2-C84
20	A1-B2-C85	A1-B2-C86	A1-B2-C87	A1-B2-C88	A1-B2-C89	A1-B2-C90
	A1-B2-C91	A1-B2-C92	A1-B2-C93	A1-B2-C94	A1-B2-C95	A1-B2-C96
	A1-B2-C97	A1-B2-C98	A1-B2-C99	A1-B2-C100	A1-B2-C101	A1-B2-C102
	A1-B2-C103	A1-B2-C104	A1-B2-C105	A1-B2-C106	A1-B2-C107	A1-B2-C108
	A1-B2-C109	A1-B2-C110	A1-B2-C111	A1-B2-C112	A1-B2-C113	A1-B2-C114
25	A1-B2-C115	A1-B2-C116	A1-B2-C117	A1-B2-C118	A1-B2-C119	A1-B2-C120
	A1-B2-C121	A1-B2-C122	A1-B2-C123	A1-B2-C124	A1-B2-C125	A1-B2-C126
	A1-B2-C127	A1-B2-C128	A1-B2-C129	A1-B2-C130	A1-B2-C131	A1-B2-C132
	A1-B2-C133	A1-B2-C134	A1-B2-C135	A1-B2-C136	A1-B2-C137	A1-B2-C138
	A1-B2-C139	A1-B2-C140	BLANK	BLANK	BLANK	BLANK
30	A1-B3-C1	A1-B3-C2	A1-B3-C3	A1-B3-C4	A1-B3-C5	A1-B3-C6
	A1-B3-C7	A1-B3-C8	A1-B3-C9	A1-B3-C10	A1-B3-C11	A1-B3-C12
	A1-B3-C13	A1-B3-C14	A1-B3-C15	A1-B3-C16	A1-B3-C17	A1-B3-C18
	A1-B3-C19	A1-B3-C20	A1-B3-C21	A1-B3-C22	A1-B3-C23	A1-B3-C24
	A1-B3-C25	A1-B3-C26	A1-B3-C27	A1-B3-C28	A1-B3-C29	A1-B3-C30
35	A1-B3-C31	A1-B3-C32	A1-B3-C33	A1-B3-C34	A1-B3-C35	A1-B3-C36
	A1-B3-C37	A1-B3-C38	A1-B3-C39	A1-B3-C40	A1-B3-C41	A1-B3-C42
	A1-B3-C43	A1-B3-C44	A1-B3-C45	A1-B3-C46	A1-B3-C47	A1-B3-C48

	A1-B3-C49	A1-B3-C50	A1-B3-C51	A1-B3-C52	A1-B3-C53	A1-B3-C54
	A1-B3-C55	A1-B3-C56	A1-B3-C57	A1-B3-C58	A1-B3-C59	A1-B3-C60
	A1-B3-C61	A1-B3-C62	A1-B3-C63	A1-B3-C64	A1-B3-C65	A1-B3-C66
	A1-B3-C67	A1-B3-C68	A1-B3-C69	A1-B3-C70	A1-B3-C71	A1-B3-C72
5	A1-B3-C73	A1-B3-C74	A1-B3-C75	A1-B3-C76	A1-B3-C77	A1-B3-C78
	A1-B3-C79	A1-B3-C80	A1-B3-C81	A1-B3-C82	A1-B3-C83	A1-B3-C84
	A1-B3-C85	A1-B3-C86	A1-B3-C87	A1-B3-C88	A1-B3-C89	A1-B3-C90
	A1-B3-C91	A1-B3-C92	A1-B3-C93	A1-B3-C94	A1-B3-C95	A1-B3-C96
	A1-B3-C97	A1-B3-C98	A1-B3-C99	A1-B3-C100	A1-B3-C101	A1-B3-C102
10	A1-B3-C103	A1-B3-C104	A1-B3-C105	A1-B3-C106	A1-B3-C107	A1-B3-C108
	A1-B3-C109	A1-B3-C110	A1-B3-C111	A1-B3-C112	A1-B3-C113	A1-B3-C114
	A1-B3-C115	A1-B3-C116	A1-B3-C117	A1-B3-C118	A1-B3-C119	A1-B3-C120
	A1-B3-C121	A1-B3-C122	A1-B3-C123	A1-B3-C124	A1-B3-C125	A1-B3-C126
	A1-B3-C127	A1-B3-C128	A1-B3-C129	A1-B3-C130	A1-B3-C131	A1-B3-C132
15	A1-B3-C133	A1-B3-C134	A1-B3-C135	A1-B3-C136	A1-B3-C137	A1-B3-C138
	A1-B3-C139	A1-B3-C140	BLANK	BLANK	BLANK	BLANK
	A1-B4-C1	A1-B4-C2 ·	A1-B4-C3	A1-B4-C4	A1-B4-C5	A1-B4-C6
	A1-B4-C7	A1-B4-C8	A1-B4-C9	A1-B4-C10	A1-B4-C11	A1-B4-C12
	A1-B4-C13	A1-B4-C14	A1-B4-C15	A1-B4-C16	A1-B4-C17	A1-B4-C18
20	A1-B4-C19	A1-B4-C20	A1-B4-C21	A1-B4-C22	A1-B4-C23	A1-B4-C24
	A1-B4-C25	A1-B4-C26	A1-B4-C27	A1-B4-C28	A1-B4-C29	A1-B4-C30
	A1-B4-C31	A1-B4-C32	A1-B4-C33	A1-B4-C34	A1-B4-C35	A1-B4-C36
	A1-B4-C37	A1-B4-C38	A1-B4-C39	A1-B4-C40	A1-B4-C41	A1-B4-C42
	A1-B4-C43	A1-B4-C44	A1-B4-C45	A1-B4-C46	A1-B4-C47	A1-B4-C48
25	A1-B4-C49	A1-B4-C50	A1-B4-C51	A1-B4-C52	A1-B4-C53	A1-B4-C54
	A1-B4-C55	A1-B4-C56	A1-B4-C57	A1-B4-C58	A1-B4-C59	A1-B4-C60
	A1-B4-C61	A1-B4-C62	A1-B4-C63	A1-B4-C64	A1-B4-C65	A1-B4-C66
	A1-B4-C67	A1-B4-C68	A1-B4-C69	A1-B4-C70	A1-B4-C71	A1-B4-C72
	A1-B4-C73	A1-B4-C74	A1-B4-C75	A1-B4-C76	A1-B4-C77	A1-B4-C78
30	A1-B4-C79	A1-B4-C80	A1-B4-C81	A1-B4-C82	A1-B4-C83	A1-B4-C84
	A1-B4-C85	A1-B4-C86	A1-B4-C87	A1-B4-C88	A1-B4-C89	A1-B4-C90
	A1-B4-C91	A1-B4-C92	A1-B4-C93	A1-B4-C94	A1-B4-C95	A1-B4-C96
	A1-B4-C97	A1-B4-C98	A1-B4-C99	A1-B4-C100	A1-B4-C101	A1-B4-C102
:	A1-B4-C103	A1-B4-C104	A1-B4-C105	A1-B4-C106	A1-B4-C107	A1-B4-C108
35	A1-B4-C109	A1-B4-C110	A1-B4-C111	A1-B4-C112	A1-B4-C113	A1-B4-C114
	A1-B4-C115	A1-B4-C116	A1-B4-C117	A1-B4-C118	A1-B4-C119	A1-B4-C120
	A1-B4-C121	A1-B4-C122	A1-B4-C123	A1-B4-C124	A1-B4-C125	A1-B4-C126

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	A1-B4-C127	A1-B4-C128	A1-B4-C129	A1-B4-C130	A1-B4-C131	A1-B4-C132
	A1-B4-C133	A1-B4-C134	A1-B4-C135	A1-B4-C136	A1-B4-C137	A1-B4-C138
	A1-B4-C139	A1-B4-C140	BLANK	BLANK	BLANK	BLANK
	A1-B5-C1	A1-B5-C2	A1-B5-C3	A1-B5-C4	A1-B5-C5	A1-B5-C6
5	A1-B5-C7	A1-B5-C8	A1-B5-C9	A1-B5-C10	A1-B5-C11	A1-B5-C12
	A1-B5-C13	A1-B5-C14	A1-B5-C15	A1-B5-C16	A1-B5-C17	A1-B5-C18
	A1-B5-C19	A1-B5-C20	A1-B5-C21	A1-B5-C22	A1-B5-C23	A1-B5-C24
	A1-B5-C25	A1-B5-C26	A1-B5-C27	A1-B5-C28	A1-B5-C29	A1-B5-C30
	A1-B5-C31	A1-B5-C32	A1-B5-C33	A1-B5-C34	A1-B5-C35	A1-B5-C36
10	A1-B5-C37	A1-B5-C38	A1-B5-C39	A1-B5-C40	A1-B5-C41	A1-B5-C42
_	A1-B5-C43	A1-B5-C44	A1-B5-C45	A1-B5-C46	A1-B5-C47	A1-B5-C48
	A1-B5-C49	A1-B5-C50	A1-B5-C51	A1-B5-C52	A1-B5-C53	A1-B5-C54
	A1-B5-C55	A1-B5-C56	A1-B5-C57	A1-B5-C58	A1-B5-C59	A1-B5-C60
	A1-B5-C61	A1-B5-C62	A1-B5-C63	A1-B5-C64	A1-B5-C65	A1-B5-C66
15	A1-B5-C67	A1-B5-C68	A1-B5-C69	A1-B5-C70	A1-B5-C71	A1-B5-C72
	A1-B5-C73	A1-B5-C74	A1-B5-C75	A1-B5-C76	A1-B5-C77	A1-B5-C78
	A1-B5-C79	A1-B5-C80	A1-B5-C81	A1-B5-C82	A1-B5-C83	A1-B5-C84
	A1-B5-C85	A1-B5-C86	A1-B5-C87	A1-B5-C88	A1-B5-C89	A1-B5-C90
	A1-B5-C91	A1-B5-C92	A1-B5-C93	A1-B5-C94	A1-B5-C95	A1-B5-C96
20	A1-B5-C97	A1-B5-C98	A1-B5-C99	A1-B5-C100	A1-B5-C101	A1-B5-C102
	A1-B5-C103	A1-B5-C104	A1-B5-C105	A1-B5-C106	A1-B5-C107	A1-B5-C108
	A1-B5-C109	A1-B5-C110	A1-B5-C111	A1-B5-C112	A1-B5-C113	A1-B5-C114
	A1-B5-C115	A1-B5-C116	A1-B5-C117	A1-B5-C118	A1-B5-C119	A1-B5-C120
	A1-B5-C121	A1-B5-C122	A1-B5-C123	A1-B5-C124	A1-B5-C125	A1-B5-C126
25	A1-B5-C127	A1-B5-C128	A1-B5-C129	A1-B5-C130	A1-B5-C131	A1-B5-C132
	A1-B5-C133	A1-B5-C134	A1-B5-C135	A1-B5-C136	A1-B5-C137	A1-B5-C138
	A1-B5-C139	A1-B5-C140	BLANK	BLANK	BLANK	BLANK
	A1-B6-C1	A1-B6-C2	A1-B6-C3	A1-B6-C4	A1-B6-C5	A1-B6-C6
	A1-B6-C7	A1-B6-C8	A1-B6-C9	A1-B6-C10	A1-B6-C11	A1-B6-C12
30	A1-B6-C13	A1-B6-C14	A1-B6-C15	A1-B6-C16	A1-B6-C17	A1-B6-C18
	A1-B6-C19	A1-B6-C20	A1-B6-C21	A1-B6-C22	A1-B6-C23	A1-B6-C24
	A1-B6-C25	A1-B6-C26	A1-B6-C27	A1-B6-C28	A1-B6-C29	A1-B6-C30
	A1-B6-C31	A1-B6-C32	A1-B6-C33	A1-B6-C34	A1-B6-C35	A1-B6-C36
	A1-B6-C37	A1-B6-C38	A1-B6-C39	A1-B6-C40	A1-B6-C41	A1-B6-C42
35	A1-B6-C43	A1-B6-C44	A1-B6-C45	A1-B6-C46	A1-B6-C47	A1-B6-C48
	A1-B6-C49	A1-B6-C50	A1-B6-C51	A1-B6-C52	A1-B6-C53	A1-B6-C54
	A1-B6-C55	A1-B6-C56	A1-B6-C57	A1-B6-C58	A1-B6-C59	A1-B6-C60

	A1-B6-C61	A1-B6-C62	A1-B6-C63	A1-B6-C64	A1-B6-C65	A1-B6-C66
	A1-B6-C67	A1-B6-C68	A1-B6-C69	A1-B6-C70	A1-B6-C71	A1-B6-C72
	A1-B6-C73	A1-B6-C74	A1-B6-C75	A1-B6-C76	A1-B6-C77	A1-B6-C78
	A1-B6-C79	A1-B6-C80	A1-B6-C81	A1-B6-C82	A1-B6-C83	A1-B6-C84
5	A1-B6-C85	A1-B6-C86	A1-B6-C87	A1-B6-C88	A1-B6-C89	A1-B6-C90
	A1-B6-C91	A1-B6-C92	A1-B6-C93	A1-B6-C94	A1-B6-C95	A1-B6-C96
	A1-B6-C97	A1-B6-C98	A1-B6-C99	A1-B6-C100	A1-B6-C101	A1-B6-C102
	A1-B6-C103	A1-B6-C104	A1-B6-C105	A1-B6-C106	A1-B6-C107	A1-B6-C108
	A1-B6-C109	A1-B6-C110	A1-B6-C111	A1-B6-C112	A1-B6-C113	A1-B6-C114
10	A1-B6-C115	A1-B6-C116	A1-B6-C117	A1-B6-C118	A1-B6-C119	A1-B6-C120
	A1-B6-C121	A1-B6-C122	A1-B6-C123	A1-B6-C124	A1-B6-C125	A1-B6-C126
	A1-B6-C127	A1-B6-C128	A1-B6-C129	A1-B6-C130	A1-B6-C131	A1-B6-C132
	A1-B6-C133	A1-B6-C134	A1-B6-C135	A1-B6-C136	A1-B6-C137	A1-B6-C138
	A1-B6-C139	A1-B6-C140	BLANK	BLANK	BLANK	BLANK
15	A1-B7-C1	A1-B7-C2	A1-B7-C3	A1-B7-C4	A1-B7-C5	A1-B7-C6
	A1-B7-C7	A1-B7-C8	A1-B7-C9	A1-B7-C10	A1-B7-C11	A1-B7-C12
	A1-B7-C13	A1-B7-C14	A1-B7-C15	A1-B7-C16	A1-B7-C17	A1-B7-C18
	A1-B7-C19	A1-B7-C20	A1-B7-C21	A1-B7-C22	A1-B7-C23	A1-B7-C24
	A1-B7-C25	A1-B7-C26	A1-B7-C27	A1-B7-C28	A1-B7-C29	A1-B7-C30
20	A1-B7-C31	A1-B7-C32	A1-B7-C33	A1-B7-C34	A1-B7-C35	A1-B7-C36
	A1-B7-C37	A1-B7-C38	A1-B7-C39	A1-B7-C40	A1-B7-C41	A1-B7-C42
	A1-B7-C43	A1-B7-C44	A1-B7-C45	A1-B7-C46	A1-B7-C47	A1-B7-C48
	A1-B7-C49	A1-B7-C50	A1-B7-C51	A1-B7-C52	A1-B7-C53	A1-B7-C54
	A1-B7-C55	A1-B7-C56	A1-B7-C57	A1-B7-C58	A1-B7-C59	A1-B7-C60
25	A1-B7-C61	A1-B7-C62	A1-B7-C63	A1-B7-C64	A1-B7-C65	A1-B7-C66
	A1-B7-C67	A1-B7-C68	A1-B7-C69	A1-B7-C70	A1-B7-C71	A1-B7-C72
	A1-B7-C73	A1-B7-C74	A1-B7-C75	A1-B7-C76	A1-B7-C77	A1-B7-C78
	A1-B7-C79	A1-B7-C80	A1-B7-C81	A1-B7-C82	A1-B7-C83	A1-B7-C84
	A1-B7-C85	A1-B7-C86	A1-B7-C87	A1-B7-C88	A1-B7-C89	A1-B7-C90
30	A1-B7-C91	A1-B7-C92	A1-B7-C93	A1-B7-C94	A1-B7-C95	A1-B7-C96
	A1-B7-C97	A1-B7-C98	A1-B7-C99	A1-B7-C100	A1-B7-C101	A1-B7-C102
	A1-B7-C103	A1-B7-C104	A1-B7-C105	A1-B7-C106	A1-B7-C107	A1-B7-C108
	A1-B7-C109	A1-B7-C110	A1-B7-C111	A1-B7-C112	A1-B7-C113	A1-B7-C114
	A1-B7-C115	A1-B7-C116	A1-B7-C117	A1-B7-C118	A1-B7-C119	A1-B7-C120
35	A1-B7-C121	A1-B7-C122	A1-B7-C123	A1-B7-C124	A1-B7-C125	A1-B7-C126
	A1-B7-C127	A1-B7-C128	A1-B7-C129	A1-B7-C130	A1-B7-C131	A1-B7-C132
	A1-B7-C133	A1-B7-C134	A1-B7-C135	A1-B7-C136	A1-B7-C137	A1-B7-C138

	A1-B7-C139	A1-B7-C140	BLANK	BLANK	BLANK	BLANK
	A1-B8-C1	A1-B8-C2	A1-B8-C3	A1-B8-C4	A1-B8-C5	A1-B8-C6
	A1-B8-C7	A1-B8-C8	A1-B8-C9	A1-B8-C10	A1-B8-C11	A1-B8-C12
	A1-B8-C13	A1-B8-C14	A1-B8-C15	A1-B8-C16	A1-B8-C17	A1-B8-C18
5	A1-B8-C19	A1-B8-C20	A1-B8-C21	A1-B8-C22	A1-B8-C23	A1-B8-C24
	A1-B8-C25	A1-B8-C26	A1-B8-C27	A1-B8-C28	A1-B8-C29	A1-B8-C30
	A1-B8-C31	A1-B8-C32	A1-B8-C33	A1-B8-C34	A1-B8-C35	A1-B8-C36
	A1-B8-C37	A1-B8-C38	A1-B8-C39	A1-B8-C40	A1-B8-C41	A1-B8-C42
	A1-B8-C43	A1-B8-C44	A1-B8-C45	A1-B8-C46	A1-B8-C47	A1-B8-C48
10	A1-B8-C49	A1-B8-C50	A1-B8-C51	A1-B8-C52	A1-B8-C53	A1-B8-C54
	A1-B8-C55	A1-B8-C56	A1-B8-C57	A1-B8-C58	A1-B8-C59	A1-B8-C60
	A1-B8-C61	A1-B8-C62	A1-B8-C63	A1-B8-C64	A1-B8-C65	A1-B8-C66
	A1-B8-C67	A1-B8-C68	A1-B8-C69	A1-B8-C70	A1-B8-C71	A1-B8-C72
	A1-B8-C73	A1-B8-C74	A1-B8-C75	A1-B8-C76	A1-B8-C77	A1-B8-C78
15	A1-B8-C79	A1-B8-C80	A1-B8-C81	A1-B8-C82	A1-B8-C83	A1-B8-C84
	A1-B8-C85	A1-B8-C86	A1-B8-C87	A1-B8-C88	A1-B8-C89	A1-B8-C90
	A1-B8-C91	A1-B8-C92	A1-B8-C93	A1-B8-C94	A1-B8-C95	A1-B8-C96
	A1-B8-C97	A1-B8-C98	A1-B8-C99	A1-B8-C100	A1-B8-C101	A1-B8-C102
	A1-B8-C103	A1-B8-C104	A1-B8-C105	A1-B8-C106	A1-B8-C107	A1-B8-C108
20	A1-B8-C109	A1-B8-C110	A1-B8-C111	A1-B8-C112	A1-B8-C113	A1-B8-C114
	A1-B8-C115	A1-B8-C116	A1-B8-C117	A1-B8-C118	A1-B8-C119	A1-B8-C120
	A1-B8-C121	A1-B8-C122	A1-B8-C123	A1-B8-C124	A1-B8-C125	A1-B8-C126
	A1-B8-C127	A1-B8-C128	A1-B8-C129	A1-B8-C130	A1-B8-C131	A1-B8-C132
	A1-B8-C133	A1-B8-C134	A1-B8-C135	A1-B8-C136	A1-B8-C137	A1-B8-C138
25	A1-B8-C139	A1-B8-C140	BLANK	BLANK	BLANK	BLANK
	A1-B9-C1	A1-B9-C2	A1-B9-C3	A1-B9-C4	A1-B9-C5	A1-B9-C6
	A1-B9-C7	A1-B9-C8	A1-B9-C9	A1-B9-C10	A1-B9-C11	A1-B9-C12
	A1-B9-C13	A1-B9-C14	A1-B9-C15	A1-B9-C16	A1-B9-C17	A1-B9-C18
	A1-B9-C19	A1-B9-C20	A1-B9-C21	A1-B9-C22	A1-B9-C23	A1-B9-C24
30	A1-B9-C25	A1-B9-C26	A1-B9-C27	A1-B9-C28	A1-B9-C29	A1-B9-C30
	A1-B9-C31	A1-B9-C32	A1-B9-C33	A1-B9-C34	A1-B9-C35	A1-B9-C36
	A1-B9-C37	A1-B9-C38	A1-B9-C39	A1-B9-C40	A1-B9-C41	A1-B9-C42
	A1-B9-C43	A1-B9-C44	A1-B9-C45	A1-B9-C46	A1-B9-C47	A1-B9-C48
	A1-B9-C49	A1-B9-C50	A1-B9-C51	A1-B9-C52	A1-B9-C53	A1-B9-C54
35	A1-B9-C55	A1-B9-C56	A1-B9-C57	A1-B9-C58	A1-B9-C59	A1-B9-C60
	A1-B9-C61	A1-B9-C62	A1-B9-C63	A1-B9-C64	A1-B9-C65	A1-B9-C66
	A1-B9-C67	A1-B9-C68	A1-B9-C69	A1-B9-C70	A1-B9-C71	A1-B9-C72

	A1-B9-C73	A1-B9-C74	A1-B9-C75	A1-B9-C76	A1-B9-C77	A1-B9-C78
	A1-B9-C79	A1-B9-C80	A1-B9-C81	A1-B9-C82	A1-B9-C83	A1-B9-C84
	A1-B9-C85	A1-B9-C86	A1-B9-C87	A1-B9-C88	A1-B9-C89	A1-B9-C90
	A1-B9-C91	A1-B9-C92	A1-B9-C93	A1-B9-C94	A1-B9-C95	A1-B9-C96
5	A1-B9-C97	A1-B9-C98	A1-B9-C99	A1-B9-C100	A1-B9-C101	A1-B9-C102
	A1-B9-C103	A1-B9-C104	A1-B9-C105	A1-B9-C106	A1-B9-C107	A1-B9-C108
	A1-B9-C109	A1-B9-C110	A1-B9-C111	A1-B9-C112	A1-B9-C113	A1-B9-C114
	A1-B9-C115	A1-B9-C116	A1-B9-C117	A1-B9-C118	A1-B9-C119	A1-B9-C120
	A1-B9-C121	A1-B9-C122	A1-B9-C123	A1-B9-C124	A1-B9-C125	A1-B9-C126
10	A1-B9-C127	A1-B9-C128	A1-B9-C129	A1-B9-C130	A1-B9-C131	A1-B9-C132
	A1-B9-C133	A1-B9-C134	A1-B9-C135	A1-B9-C136	A1-B9-C137	A1-B9-C138
	A1-B9-C139	A1-B9-C140	BLANK	BLANK	BLANK	BLANK
	A1-B10-C1	A1-B10-C2	A1-B10-C3	A1-B10-C4	A1-B10-C5	A1-B10-C6
	A1-B10-C7	A1-B10-C8	A1-B10-C9	A1-B10-C10	A1-B10-C11	A1-B10-C12
15	A1-B10-C13	A1-B10-C14	A1-B10-C15	A1-B10-C16	A1-B10-C17	A1-B10-C18
	A1-B10-C19	A1-B10-C20	A1-B10-C21	A1-B10-C22	A1-B10-C23	A1-B10-C24
	A1-B10-C25	A1-B10-C26	A1-B10-C27	A1-B10-C28	A1-B10-C29	A1-B10-C30
	A1-B10-C31	A1-B10-C32	A1-B10-C33	A1-B10-C34	A1-B10-C35	A1-B10-C36
	A1-B10-C37	A1-B10-C38	A1-B10-C39	A1-B10-C40	A1-B10-C41	A1-B10-C42
20	A1-B10-C43	A1-B10-C44	A1-B10-C45	A1-B10-C46	A1-B10-C47	A1-B10-C48
	A1-B10-C49	A1-B10-C50	A1-B10-C51	A1-B10-C52	A1-B10-C53	A1-B10-C54
	A1-B10-C55	A1-B10-C56	A1-B10-C57	A1-B10-C58	A1-B10-C59	A1-B10-C60
	A1-B10-C61	A1-B10-C62	A1-B10-C63	A1-B10-C64	A1-B10-C65	A1-B10-C66
	A1-B10-C67	A1-B10-C68	A1-B10-C69	A1-B10-C70	A1-B10-C71	A1-B10-C72
25	A1-B10-C73	A1-B10-C74	A1-B10-C75	A1-B10-C76	A1-B10-C77	A1-B10-C78
	A1-B10-C79	A1-B10-C80	A1-B10-C81	A1-B10-C82	A1-B10-C83	A1-B10-C84
	A1-B10-C85	A1-B10-C86	A1-B10-C87	A1-B10-C88	A1-B10-C89	A1-B10-C90
	A1-B10-C91	A1-B10-C92	A1-B10-C93	A1-B10-C94	A1-B10-C95	A1-B10-C96
	A1-B10-C97	A1-B10-C98	A1-B10-C99	A1-B10-C100	A1-B10-C101	A1-B10-C102
30	A1-B10-C103	A1-B10-C104	A1-B10-C105	A1-B10-C106	A1-B10-C107	A1-B10-C108
	A1-B10-C109	A1-B10-C110	A1-B10-C111	A1-B10-C112	A1-B10-C113	A1-B10-C114
	A1-B10-C115	A1-B10-C116	A1-B10-C117	A1-B10-C118	A1-B10-C119	A1-B10-C120
	A1-B10-C121	A1-B10-C122	A1-B10-C123	A1-B10-C124	A1-B10-C125	A1-B10-C126
	A1-B10-C127	A1-B10-C128	A1-B10-C129	A1-B10-C130	A1-B10-C131	A1-B10-C132
35	A1-B10-C133	A1-B10-C134	A1-B10-C135	A1-B10-C136	A1-B10-C137	A1-B10-C138
	A1-B10-C139	A1-B10-C140	BLANK	BLANK	BLANK	BLANK
	A1-B11-C1	A1-B11-C2	A1-B11-C3	A1-B11-C4	A1-B11-C5	A1-B11-C6

	A1-B11-C7	A1-B11-C8	A1-B11-C9	A1-B11-C10	A1-B11-C11	A1-B11-C12
	A1-B11-C13	A1-B11-C14	A1-B11-C15	A1-B11-C16	A1-B11-C17	A1-B11-C18
	A1-B11-C19	A1-B11-C20	A1-B11-C21	A1-B11-C22	A1-B11-C23	A1-B11-C24
	A1-B11-C25	A1-B11-C26	A1-B11-C27	A1-B11-C28	A1-B11-C29	A1-B11-C30
5	A1-B11-C31	A1-B11-C32	A1-B11-C33	A1-B11-C34	A1-B11-C35	A1-B11-C36
	A1-B11-C37	A1-B11-C38	A1-B11-C39	A1-B11-C40	A1-B11-C41	A1-B11-C42
	A1-B11-C43	A1-B11-C44	A1-B11-C45	A1-B11-C46	A1-B11-C47	A1-B11-C48
	A1-B11-C49	A1-B11-C50	A1-B11-C51	A1-B11-C52	A1-B11-C53	A1-B11-C54
	A1-B11-C55	A1-B11-C56	A1-B11-C57	A1-B11-C58	A1-B11-C59	A1-B11-C60
10	A1-B11-C61	A1-B11-C62	A1-B11-C63	A1-B11-C64	A1-B11-C65	A1-B11-C66
	A1-B11-C67	A1-B11-C68	A1-B11-C69	A1-B11-C70	A1-B11-C71	A1-B11-C72
	A1-B11-C73	A1-B11-C74	A1-B11-C75	A1-B11-C76	A1-B11-C77	A1-B11-C78
	A1-B11-C79	A1-B11-C80	A1-B11-C81	A1-B11-C82	A1-B11-C83	A1-B11-C84
	A1-B11-C85	A1-B11-C86	A1-B11-C87	A1-B11-C88	A1-B11-C89	A1-B11-C90
15	A1-B11-C91	A1-B11-C92	A1-B11-C93	A1-B11-C94	A1-B11-C95	A1-B11-C96
	A1-B11-C97	A1-B11-C98	A1-B11-C99	A1-B11-C100	A1-B11-C101	A1-B11-C102
	A1-B11-C103	A1-B11-C104	A1-B11-C105	A1-B11-C106	A1-B11-C107	A1-B11-C108
	A1-B11-C109	A1-B11-C110	A1-B11-C111	A1-B11-C112	A1-B11-C113	A1-B11-C114
	A1-B11-C115	A1-B11-C116	A1-B11-C117	A1-B11-C118	A1-B11-C119	A1-B11-C120
20	A1-B11-C121	A1-B11-C122	A1-B11-C123	A1-B11-C124	A1-B11-C125	A1-B11-C126
	A1-B11-C127	A1-B11-C128	A1-B11-C129	A1-B11-C130	A1-B11-C131	A1-B11-C132
	A1-B11-C133	A1-B11-C134	A1-B11-C135	A1-B11-C136	A1-B11-C137	A1-B11-C138
	A1-B11-C139	A1-B11-C140	BLANK	BLANK	BLANK	BLANK
	A1-B12-C1	A1-B12-C2	A1-B12-C3	A1-B12-C4	A1-B12-C5	A1-B12-C6
25	A1-B12-C7	A1-B12-C8	A1-B12-C9	A1-B12-C10	A1-B12-C11	A1-B12-C12
	A1-B12-C13	A1-B12-C14	A1-B12-C15	A1-B12-C16	A1-B12-C17	A1-B12-C18
	A1-B12-C19	A1-B12-C20	A1-B12-C21	A1-B12-C22	A1-B12-C23	A1-B12-C24
	A1-B12-C25	A1-B12-C26	A1-B12-C27	A1-B12-C28	A1-B12-C29	A1-B12-C30
	A1-B12-C31	A1-B12-C32	A1-B12-C33	A1-B12-C34	A1-B12-C35	A1-B12-C36
30	A1-B12-C37	A1-B12-C38	A1-B12-C39	A1-B12-C40	A1-B12-C41	A1-B12-C42
	A1-B12-C43	A1-B12-C44	A1-B12-C45	A1-B12-C46	A1-B12-C47	A1-B12-C48
	A1-B12-C49	A1-B12-C50	A1-B12-C51	A1-B12-C52	A1-B12-C53	A1-B12-C54
	A1-B12-C55	A1-B12-C56	A1-B12-C57	A1-B12-C58	A1-B12-C59	A1-B12-C60
	A1-B12-C61	A1-B12-C62	A1-B12-C63	A1-B12-C64	A1-B12-C65	A1-B12-C66
35	A1-B12-C67	A1-B12-C68	A1-B12-C69	A1-B12-C70	A1-B12-C71	A1-B12-C72
	A1-B12-C73	A1-B12-C74	A1-B12-C75	A1-B12-C76	A1-B12-C77	A1-B12-C78
	A1-B12-C79	A1-B12-C80	A1-B12-C81	A1-B12-C82	A1-B12-C83	A1-B12-C84

	A1-B12-C85	A1-B12-C86	A1-B12-C87	A1-B12-C88	A1-B12-C89	A1-B12-C90
	AI-B12-C91	A1-B12-C92	A1-B12-C93	A1-B12-C94	A1-B12-C95	A1-B12-C96
	A1-B12-C97	A1-B12-C98	A1-B12-C99	A1-B12-C100	A1-B12-C101	A1-B12-C102
	A1-B12-C103	A1-B12-C104	A1-B12-C105	A1-B12-C106	A1-B12-C107	A1-B12-C108
5	A1-B12-C109	A1-B12-C110	A1-B12-C111	A1-B12-C112	A1-B12-C113	A1-B12-C114
	A1-B12-C115	A1-B12-C116	A1-B12-C117	A1-B12-C118	A1-B12-C119	A1-B12-C120
	A1-B12-C121	A1-B12-C122	A1-B12-C123	A1-B12-C124	A1-B12-C125	A1-B12-C126
	A1-B12-C127	A1-B12-C128	A1-B12-C129	A1-B12-C130	A1-B12-C131	A1-B12-C132
	A1-B12-C133	A1-B12-C134	A1-B12-C135	A1-B12-C136	A1-B12-C137	A1-B12-C138
10	A1-B12-C139	A1-B12-C140	BLANK	BLANK	BLANK	BLANK
	A1-B13-C1	A1-B13-C2	A1-B13-C3	A1-B13-C4	A1-B13-C5	A1-B13-C6
	A1-B13-C7	A1-B13-C8	A1-B13-C9	A1-B13-C10	A1-B13-C11	A1-B13-C12
	A1-B13-C13	A1-B13-C14	A1-B13-C15	A1-B13-C16	A1-B13-C17	A1-B13-C18
	A1-B13-C19	A1-B13-C20	A1-B13-C21	A1-B13-C22	A1-B13-C23	A1-B13-C24
15	A1-B13-C25	A1-B13-C26	A1-B13-C27	A1-B13-C28	A1-B13-C29	A1-B13-C30
	A1-B13-C31	A1-B13-C32	A1-B13-C33	A1-B13-C34	A1-B13-C35	A1-B13-C36
	A1-B13-C37	A1-B13-C38	A1-B13-C39	A1-B13-C40	A1-B13-C41	A1-B13-C42
	A1-B13-C43	A1-B13-C44	A1-B13-C45	A1-B13-C46	A1-B13-C47	A1-B13-C48
	A1-B13-C49	A1-B13-C50	A1-B13-C51	A1-B13-C52	A1-B13-C53	A1-B13-C54
20	A1-B13-C55	A1-B13-C56	A1-B13-C57	A1-B13-C58	A1-B13-C59	A1-B13-C60
	A1-B13-C61	A1-B13-C62	A1-B13-C63	A1-B13-C64	A1-B13-C65	A1-B13-C66
	A1-B13-C67	A1-B13-C68	A1-B13-C69	A1-B13-C70	A1-B13-C71	A1-B13-C72
	A1-B13-C73	A1-B13-C74	A1-B13-C75	A1-B13-C76	A1-B13-C77	A1-B13-C78
	A1-B13-C79	A1-B13-C80	A1-B13-C81	A1-B13-C82	A1-B13-C83	A1-B13-C84
25	A1-B13-C85	A1-B13-C86	A1-B13-C87	A1-B13-C88	A1-B13-C89	A1-B13-C90
	A1-B13-C91	A1-B13-C92	A1-B13-C93	A1-B13-C94	A1-B13-C95	A1-B13-C96
	A1-B13-C97	A1-B13-C98	A1-B13-C99	A1-B13-C100	A1-B13-C101	A1-B13-C102
	A1-B13-C103	A1-B13-C104	A1-B13-C105	A1-B13-C106	A1-B13-C107	A1-B13-C108
	A1-B13-C109	A1-B13-C110	A1-B13-C111	A1-B13-C112	A1-B13-C113	A1-B13-C114
30	A1-B13-C115	A1-B13-C116	A1-B13-C117	A1-B13-C118	A1-B13-C119	A1-B13-C120
	A1-B13-C121	A1-B13-C122	A1-B13-C123	A1-B13-C124	A1-B13-C125	A1-B13-C126
	A1-B13-C127	A1-B13-C128	A1-B13-C129	A1-B13-C130	A1-B13-C131	A1-B13-C132
	A1-B13-C133	A1-B13-C134	A1-B13-C135	A1-B13-C136	A1-B13-C137	A1-B13-C138
	A1-B13-C139	A1-B13-C140	BLANK	BLANK	BLANK	BLANK
35	A2-B1-C1	A2-B1-C2	A2-B1-C3	A2-B1-C4	A2-B1-C5	A2-B1-C6
	A2-B1-C7	A2-B1-C8	A2-B1-C9	A2-B1-C10	A2-B1-C11	A2-B1-C12
	A2-B1-C13	A2-B1-C14	A2-B1-C15	A2-B1-C16	A2-B1-C17	A2-B1-C18

	A2-B1-C19	A2-B1-C20	A2-B1-C21	A2-B1-C22	A2-B1-C23	A2-B1-C24
	A2-B1-C25	A2-B1-C26	A2-B1-C27	A2-B1-C28	A2-B1-C29	A2-B1-C30
	A2-B1-C31	A2-B1-C32	A2-B1-C33	A2-B1-C34	A2-B1-C35	A2-B1-C36
	A2-B1-C37	A2-B1-C38	A2-B1-C39	A2-B1-C40	A2-B1-C41	A2-B1-C42
5	A2-B1-C43	A2-B1-C44	A2-B1-C45	A2-B1-C46	A2-B1-C47	A2-B1-C48
	A2-B1-C49	A2-B1-C50	A2-B1-C51	A2-B1-C52	A2-B1-C53	A2-B1-C54
	A2-B1-C55	A2-B1-C56	A2-B1-C57	A2-B1-C58	A2-B1-C59	A2-B1-C60
	A2-B1-C61	A2-B1-C62	A2-B1-C63	A2-B1-C64	A2-B1-C65	A2-B1-C66
	A2-B1-C67	A2-B1-C68	A2-B1-C69	A2-B1-C70	A2-B1-C71	A2-B1-C72
10	A2-B1-C73	A2-B1-C74	A2-B1-C75	A2-B1-C76	A2-B1-C77	A2-B1-C78
	A2-B1-C79	A2-B1-C80	A2-B1-C81	A2-B1-C82	A2-B1-C83	A2-B1-C84
	A2-B1-C85	A2-B1-C86	A2-B1-C87	A2-B1-C88	A2-B1-C89	A2-B1-C90
	A2-B1-C91	A2-B1-C92	A2-B1-C93	A2-B1-C94	A2-B1-C95	A2-B1-C96
	A2-B1-C97	A2-B1-C98	A2-B1-C99	A2-B1-C100	A2-B1-C101	A2-B1-C102
15	A2-B1-C103	A2-B1-C104	A2-B1-C105	A2-B1-C106	A2-B1-C107	A2-B1-C108
	A2-B1-C109	A2-B1-C110	A2-B1-C111	A2-B1-C112	A2-B1-C113	A2-B1-C114
	A2-B1-C115	A2-B1-C116	A2-B1-C117	A2-B1-C118	A2-B1-C119	A2-B1-C120
	A2-B1-C121	A2-B1-C122	A2-B1-C123	A2-B1-C124	A2-B1-C125	A2-B1-C126
	A2-B1-C127	A2-B1-C128	A2-B1-C129	A2-B1-C130	A2-B1-C131	A2-B1-C132
20	A2-B1-C133	A2-B1-C134	A2-B1-C135	A2-B1-C136	A2-B1-C137	A2-B1-C138
	A2-B1-C139	A2-B1-C140	BLANK	BLANK	BLANK	BLANK
	A2-B2-C1	A2-B2-C2	A2-B2-C3	A2-B2-C4	A2-B2-C5	A2-B2-C6
	A2-B2-C7	A2-B2-C8	A2-B2-C9	A2-B2-C10	A2-B2-C11	A2-B2-C12
	A2-B2-C13	A2-B2-C14	A2-B2-C15	A2-B2-C16	A2-B2-C17	A2-B2-C18
25	A2-B2-C19	A2-B2-C20	A2-B2-C21	A2-B2-C22	A2-B2-C23	A2-B2-C24
	A2-B2-C25	A2-B2-C26	A2-B2-C27	A2-B2-C28	A2-B2-C29	A2-B2-C30
	A2-B2-C31	A2-B2-C32	A2-B2-C33	A2-B2-C34	A2-B2-C35	A2-B2-C36
	A2-B2-C37	A2-B2-C38	A2-B2-C39	A2-B2-C40	A2-B2-C41	A2-B2-C42
	A2-B2-C43	A2-B2-C44	A2-B2-C45	A2-B2-C46	A2-B2-C47	A2-B2-C48
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	A2-B2-C85	A2-B2-C86	A2-B2-C87	A2-B2-C88	A2-B2-C89	A2-B2-C90
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	A2-B2-C103	A2-B2-C104	A2-B2-C105	A2-B2-C106	A2-B2-C107	A2-B2-C108
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	A2-B2-C115	A2-B2-C116	A2-B2-C117	A2-B2-C118	A2-B2-C119	A2-B2-C120
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	A2-B2-C127	A2-B2-C128	A2-B2-C129	A2-B2-C130	A2-B2-C131	A2-B2-C132
	A2-B2-C133	A2-B2-C134	A2-B2-C135 ·	A2-B2-C136	A2-B2-C137	A2-B2-C138
	A2-B2-C139	A2-B2-C140	BLANK	BLANK	BLANK	BLANK
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	A2-B3-C13	A2-B3-C14	A2-B3-C15	A2-B3-C16	A2-B3-C17	A2-B3-C18
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	A2-B3-C25	A2-B3-C26	A2-B3-C27	A2-B3-C28	A2-B3-C29	A2-B3-C30
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	A2-B3-C49	A2-B3-C50	A2-B3-C51	A2-B3-C52	A2-B3-C53	A2-B3-C54
	A2-B3-C55	A2-B3-C56	A2-B3-C57	A2-B3-C58	A2-B3-C59	A2-B3-C60
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	A2-B3-C103	A2-B3-C104	A2-B3-C105	A2-B3-C106	A2-B3-C107	A2-B3-C108
	A2-B3-C109	A2-B3-C110	A2-B3-C111	A2-B3-C112	A2-B3-C113	A2-B3-C114
	A2-B3-C115	A2-B3-C116	A2-B3-C117	A2-B3-C118	A2-B3-C119	A2-B3-C120
	A2-B3-C121	A2-B3-C122	A2-B3-C123	A2-B3-C124	A2-B3-C125	A2-B3-C126
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	A2-B3-C133	A2-B3-C134	A2-B3-C135	A2-B3-C136	A2-B3-C137	A2-B3-C138
	A2-B3-C139	A2-B3-C140	BLANK	BLANK	BLANK	BLANK
	A2-B4-C1	A2-B4-C2	A2-B4-C3	A2-B4-C4	A2-B4-C5	A2-B4-C6
	A2-B4-C7	A2-B4-C8	A2-B4-C9	A2-B4-C10	A2-B4-C11	A2-B4-C12
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	A2-B4-C19	A2-B4-C20	A2-B4-C21	A2-B4-C22	A2-B4-C23	A2-B4-C24
	A2-B4-C25	A2-B4-C26	A2-B4-C27	A2-B4-C28	A2-B4-C29	A2-B4-C30

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	A2-B4-C43	A2-B4-C44	A2-B4-C45	A2-B4-C46	A2-B4-C47	A2-B4-C48
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	A2-B4-C79	A2-B4-C80	A2-B4-C81	A2-B4-C82	A2-B4-C83	A2-B4-C84
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	A2-B4-C103	A2-B4-C104	A2-B4-C105	A2-B4-C106	A2-B4-C107	A2-B4-C108
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	A2-B4-C127	A2-B4-C128	A2-B4-C129	A2-B4-C130	A2-B4-C131	A2-B4-C132
	A2-B4-C133	A2-B4-C134	A2-B4-C135	A2-B4-C136	A2-B4-C137	A2-B4-C138
	A2-B4-C139	A2-B4-C140	BLANK	BLANK	BLANK	BLANK
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	A2-B5-C13	A2-B5-C14	A2-B5-C15	A2-B5-C16	A2-B5-C17	A2-B5-C18
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	A2-B5-C25	A2-B5-C26	A2-B5-C27	A2-B5-C28	A2-B5-C29	A2-B5-C30
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	A2-B5-C55	A2-B5-C56	A2-B5-C57	A2-B5-C58	A2-B5-C59	A2-B5-C60
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	A2-B5-C73	A2-B5-C74	A2-B5-C75	A2-B5-C76	A2-B5-C77	A2-B5-C78
	A2-B5-C79	A2-B5-C80	A2-B5-C81	A2-B5-C82	A2-B5-C83	A2-B5-C84
	A2-B5-C85	A2-B5-C86	A2-B5-C87	A2-B5-C88	A2-B5-C89	A2-B5-C90
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	A2-B5-C97	A2-B5-C98	A2-B5-C99	A2-B5-C100	A2-B5-C101	A2-B5-C102
	A2-B5-C103	A2-B5-C104	A2-B5-C105	A2-B5-C106	A2-B5-C107	A2-B5-C108

	A2-B5-C109	A2-B5-C110	A2-B5-C111	A2-B5-C112	A2-B5-C113	A2-B5-C114
	A2-B5-C115	A2-B5-C116	A2-B5-C117	A2-B5-C118	A2-B5-C119	A2-B5-C120
	A2-B5-C121	A2-B5-C122	A2-B5-C123	A2-B5-C124	A2-B5-C125	A2-B5-C126
	A2-B5-C127	A2-B5-C128	A2-B5-C129	A2-B5-C130	A2-B5-C131	A2-B5-C132
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	A2-B5-C139	A2-B5-C140	BLANK	BLANK .	BLANK	BLANK
	A2-B6-C1	A2-B6-C2	A2-B6-C3	A2-B6-C4	A2-B6-C5	A2-B6-C6
	A2-B6-C7	A2-B6-C8	A2-B6-C9	A2-B6-C10	A2-B6-C11	A2-B6-C12
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-	A2-B6-C25	A2-B6-C26	A2-B6-C27	A2-B6-C28	A2-B6-C29	A2-B6-C30
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	A2-B6-C37	A2-B6-C38	A2-B6-C39	A2-B6-C40	A2-B6-C41	A2-B6-C42
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	A2-B6-C61	A2-B6-C62	A2-B6-C63	A2-B6-C64	A2-B6-C65	A2-B6-C66
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	A2-B6-C103	A2-B6-C104	A2-B6-C105	A2-B6-C106	A2-B6-C107	A2-B6-C108
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	A2-B6-C115	A2-B6-C116	A2-B6-C117	A2-B6-C118	A2-B6-C119	A2-B6-C120
	A2-B6-C121	A2-B6-C122	A2-B6-C123	A2-B6-C124	A2-B6-C125	A2-B6-C126
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	A2-B6-C133	A2-B6-C134	A2-B6-C135	A2-B6-C136	A2-B6-C137	A2-B6-C138
30	A2-B6-C139	A2-B6-C140	BLANK	BLANK	BLANK	BLANK
	A2-B7-C1	A2-B7-C2	A2-B7-C3	A2-B7-C4	A2-B7-C5	A2-B7-C6
	A2-B7-C7	A2-B7-C8	A2-B7-C9	A2-B7-C10	A2-B7-C11	A2-B7-C12
	A2-B7-C13	A2-B7-C14	A2-B7-C15	A2-B7-C16	A2-B7-C17	A2-B7-C18
	A2-B7-C19	A2-B7-C20	A2-B7-C21	A2-B7-C22	A2-B7-C23	A2-B7-C24
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	A2-B7-C31	A2-B7-C32	A2-B7-C33	A2-B7-C34	A2-B7-C35	A2-B7-C36
	A2-B7-C37	A2-B7-C38	A2-B7-C39	A2-B7-C40	A2-B7-C41	A2-B7-C42

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	A2-B7-C55	A2-B7-C56	A2-B7-C57	A2-B7-C58	A2-B7-C59	A2-B7-C60
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	A2-B7-C79	A2-B7-C80	A2-B7-C81	A2-B7-C82	A2-B7-C83	A2-B7-C84
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	A2-B7-C91	A2-B7-C92	A2-B7-C93	A2-B7-C94	A2-B7-C95	A2-B7-C96
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	A2-B7-C103	A2-B7-C104	A2-B7-C105	A2-B7-C106	A2-B7-C107	A2-B7-C108
	A2-B7-C109	A2-B7-C110	A2-B7-C111	A2-B7-C112	A2-B7-C113	A2-B7-C114
	A2-B7-C115	A2-B7-C116	A2-B7-C117	A2-B7-C118	A2-B7-C119	A2-B7-C120
	A2-B7-C121	A2-B7-C122	A2-B7-C123	A2-B7-C124	A2-B7-C125	A2-B7-C126
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	A2-B7-C133	A2-B7-C134	A2-B7-C135	A2-B7-C136	A2-B7-C137	A2-B7-C138
	A2-B7-C139	A2-B7-C140	BLANK	BLANK	BLANK	BLANK
	A2-B8-C1	A2-B8-C2	A2-B8-C3	A2-B8-C4	A2-B8-C5	A2-B8-C6
	A2-B8-C7	A2-B8-C8	A2-B8-C9	A2-B8-C10	A2-B8-C11	A2-B8-C12
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	A2-B8-C19	A2-B8-C20	A2-B8-C21	A2-B8-C22	A2-B8-C23	A2-B8-C24
	A2-B8-C25	A2-B8-C26	A2-B8-C27	A2-B8-C28	A2-B8-C29	A2-B8-C30
	A2-B8-C31	A2-B8-C32	A2-B8-C33	A2-B8-C34	A2-B8-C35	A2-B8-C36
	A2-B8-C37	A2-B8-C38	A2-B8-C39	A2-B8-C40	A2-B8-C41	A2-B8-C42
25	A2-B8-C43	A2-B8-C44	A2-B8-C45	A2-B8-C46	A2-B8-C47	A2-B8-C48
	A2-B8-C49	A2-B8-C50	A2-B8-C51	A2-B8-C52	A2-B8-C53	A2-B8-C54
	A2-B8-C55	A2-B8-C56	A2-B8-C57	A2-B8-C58	A2-B8-C59	A2-B8-C60
	A2-B8-C61	A2-B8-C62	A2-B8-C63	A2-B8-C64	A2-B8-C65	A2-B8-C66
	A2-B8-C67	A2-B8-C68	A2-B8-C69	A2-B8-C70	A2-B8-C71	A2-B8-C72
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	A2-B8-C79	A2-B8-C80	A2-B8-C81	A2-B8-C82	A2-B8-C83	A2-B8-C84
	A2-B8-C85	A2-B8-C86	A2-B8-C87	A2-B8-C88	A2-B8-C89	A2-B8-C90
	A2-B8-C91	A2-B8-C92	A2-B8-C93	A2-B8-C94	A2-B8-C95	A2-B8-C96
	A2-B8-C97	A2-B8-C98	A2-B8-C99	A2-B8-C100	A2-B8-C101	A2-B8-C102
35	A2-B8-C103	A2-B8-C104	A2-B8-C105	A2-B8-C106	A2-B8-C107	A2-B8-C108
	A2-B8-C109	A2-B8-C110	A2-B8-C111	A2-B8-C112	A2-B8-C113	A2-B8-C114
	A2-B8-C115	A2-B8-C116	A2-B8-C117	A2-B8-C118	A2-B8-C119	A2-B8-C120

	A2-B8-C121	A2-B8-C122	A2-B8-C123	A2-B8-C124	A2-B8-C125	A2-B8-C126
	A2-B8-C127	A2-B8-C128	A2-B8-C129	A2-B8-C130	A2-B8-C131	A2-B8-C132
	A2-B8-C133	A2-B8-C134	A2-B8-C135	A2-B8-C136	A2-B8-C137	A2-B8-C138
	A2-B8-C139	A2-B8-C140	BLANK	BLANK	BLANK	BLANK
5	A2-B9-C1	A2-B9-C2	A2-B9-C3	A2-B9-C4	A2-B9-C5	A2-B9-C6
	A2-B9-C7	A2-B9-C8	A2-B9-C9	A2-B9-C10	A2-B9-C11	A2-B9-C12
	A2-B9-C13	A2-B9-C14	A2-B9-C15	A2-B9-C16	A2-B9-C17	A2-B9-C18
	A2-B9-C19	A2-B9-C20	A2-B9-C21	A2-B9-C22	A2-B9-C23	A2-B9-C24
	A2-B9-C25	A2-B9-C26	A2-B9-C27	A2-B9-C28	A2-B9-C29	A2-B9-C30
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	A2-B9-C37	A2-B9-C38	A2-B9-C39	A2-B9-C40	A2-B9-C41	A2-B9-C42
	A2-B9-C43	A2-B9-C44	A2-B9-C45	A2-B9-C46	A2-B9-C47	A2-B9-C48
	A2-B9-C49	A2-B9-C50	A2-B9-C51	A2-B9-C52	A2-B9-C53	A2-B9-C54
	A2-B9-C55	A2-B9-C56	A2-B9-C57	A2-B9-C58	A2-B9-C59	A2-B9-C60
15 ·	A2-B9-C61	A2-B9-C62	A2-B9-C63	A2-B9-C64	A2-B9-C65	A2-B9-C66
	A2-B9-C67	A2-B9-C68	A2-B9-C69	A2-B9-C70	A2-B9-C71	A2-B9-C72
	A2-B9-C73	A2-B9-C74	A2-B9-C75	A2-B9-C76	A2-B9-C77	A2-B9-C78
	A2-B9-C79	A2-B9-C80	A2-B9-C81	A2-B9-C82	A2-B9-C83	A2-B9-C84
	A2-B9-C85	A2-B9-C86	A2-B9-C87	A2-B9-C88	A2-B9-C89	A2-B9-C90
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	A2-B9-C97	A2-B9-C98	A2-B9-C99	A2-B9-C100	A2-B9-C101	A2-B9-C102
	A2-B9-C103	A2-B9-C104	A2-B9-C105	A2-B9-C106	A2-B9-C107	A2-B9-C108
	A2-B9-C109	A2-B9-C110	A2-B9-C111	A2-B9-C112	A2-B9-C113	A2-B9-C114
	A2-B9-C115	A2-B9-C116	A2-B9-C117	A2-B9-C118	A2-B9-C119	A2-B9-C120
25	A2-B9-C121	A2-B9-C122	A2-B9-C123	A2-B9-C124	A2-B9-C125	A2-B9-C126
	A2-B9-C127	A2-B9-C128	A2-B9-C129	A2-B9-C130	A2-B9-C131	A2-B9-C132
	A2-B9-C133	A2-B9-C134	A2-B9-C135	A2-B9-C136	A2-B9-C137	A2-B9-C138
	A2-B9-C139	A2-B9-C140	BLANK	BLANK	BLANK	BLANK
	A2-B10-C1	A2-B10-C2	A2-B10-C3	A2-B10-C4	A2-B10-C5	A2-B10-C6
30	A2-B10-C7	A2-B10-C8	A2-B10-C9	A2-B10-C10	A2-B10-C11	A2-B10-C12
	A2-B10-C13	A2-B10-C14	A2-B10-C15	A2-B10-C16	A2-B10-C17	A2-B10-C18
	A2-B10-C19	A2-B10-C20	A2-B10-C21	A2-B10-C22	A2-B10-C23	A2-B10-C24
	A2-B10-C25	A2-B10-C26	A2-B10-C27	A2-B10-C28	A2-B10-C29	A2-B10-C30
	A2-B10-C31	A2-B10-C32	A2-B10-C33	A2-B10-C34	A2-B10-C35	A2-B10-C36
35	A2-B10-C37	A2-B10-C38	A2-B10-C39	A2-B10-C40	A2-B10-C41	A2-B10-C42
	A2-B10-C43	A2-B10-C44	A2-B10-C45	A2-B10-C46	A2-B10-C47	A2-B10-C48
	A2-B10-C49	A2-B10-C50	A2-B10-C51	A2-B10-C52	A2-B10-C53	A2-B10-C54

	A2-B10-C55	A2-B10-C56	A2-B10-C57	A2-B10-C58	A2-B10-C59	A2-B10-C60
	A2-B10-C61	A2-B10-C62	A2-B10-C63	A2-B10-C64	A2-B10-C65	A2-B10-C66
	A2-B10-C67	A2-B10-C68	A2-B10-C69	A2-B10-C70	A2-B10-C71	A2-B10-C72
	A2-B10-C73	A2-B10-C74	A2-B10-C75	A2-B10-C76	A2-B10-C77	A2-B10-C78
5	A2-B10-C79	A2-B10-C80	A2-B10-C81	A2-B10-C82	A2-B10-C83	A2-B10-C84
	A2-B10-C85	A2-B10-C86	A2-B10-C87	A2-B10-C88	A2-B10-C89	A2-B10-C90
	A2-B10-C91	A2-B10-C92	A2-B10-C93	A2-B10-C94	A2-B10-C95	A2-B10-C96
	A2-B10-C97	A2-B10-C98	A2-B10-C99	A2-B10-C100	A2-B10-C101	A2-B10-C102
	A2-B10-C103	A2-B10-C104	A2-B10-C105	A2-B10-C106	A2-B10-C107	A2-B10-C108
10	A2-B10-C109	A2-B10-C110	A2-B10-C111	A2-B10-C112	A2-B10-C113	A2-B10-C114
	A2-B10-C115	A2-B10-C116	A2-B10-C117	A2-B10-C118	A2-B10-C119	A2-B10-C120
	A2-B10-C121	A2-B10-C122	A2-B10-C123	A2-B10-C124	A2-B10-C125	A2-B10-C126
	A2-B10-C127	A2-B10-C128	A2-B10-C129	A2-B10-C130	A2-B10-C131	A2-B10-C132
	A2-B10-C133	A2-B10-C134	A2-B10-C135	A2-B10-C136	A2-B10-C137	A2-B10-C138
15	A2-B10-C139	A2-B10-C140	BLANK	BLANK	BLANK	BLANK
	A2-B11-C1	A2-B11-C2	A2-B11-C3	A2-B11-C4	A2-B11-C5	A2-B11-C6
	A2-B11-C7	A2-B11-C8	A2-B11-C9	A2-B11-C10	A2-B11-C11	A2-B11-C12
	A2-B11-C13	A2-B11-C14	A2-B11-C15	A2-B11-C16	A2-B11-C17	A2-B11-C18
	A2-B11-C19	A2-B11-C20	A2-B11-C21	A2-B11-C22	A2-B11-C23	A2-B11-C24
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	A2-B11-C31	A2-B11-C32	A2-B11-C33	A2-B11-C34	A2-B11-C35	A2-B11-C36
	A2-B11-C37	A2-B11-C38	A2-B11-C39	A2-B11-C40	A2-B11-C41	A2-B11-C42
	A2-B11-C43	A2-B11-C44	A2-B11-C45	A2-B11-C46	A2-B11-C47	A2-B11-C48
	A2-B11-C49	A2-B11-C50	A2-B11-C51	A2-B11-C52	A2-B11-C53	A2-B11-C54
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	A2-B11-C61	A2-B11-C62	A2-B11-C63	A2-B11-C64	A2-B11-C65	A2-B11-C66
	A2-B11-C67	A2-B11-C68	A2-B11-C69	A2-B11-C70	A2-B11-C71	A2-B11-C72
	A2-B11-C73	A2-B11-C74	A2-B11-C75	A2-B11-C76	A2-B11-C77	A2-B11-C78
	A2-B11-C79	A2-B11-C80	A2-B11-C81	A2-B11-C82	A2-B11-C83	A2-B11-C84
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	A2-B11-C97	A2-B11-C98	A2-B11-C99	A2-B11-C100	A2-B11-C101	A2-B11-C102
	A2-B11-C103	A2-B11-C104	A2-B11-C105	A2-B11-C106	A2-B11-C107	A2-B11-C108
	A2-B11-C109	A2-B11-C110	A2-B11-C111	A2-B11-C112	A2-B11-C113	A2-B11-C114
35	A2-B11-C115	A2-B11-C116	A2-B11-C117	A2-B11-C118	A2-B11-C119	A2-B11-C120
	A2-B11-C121	A2-B11-C122	A2-B11-C123	A2-B11-C124	A2-B11-C125	A2-B11-C126
	A2-B11-C127	A2-B11-C128	A2-B11-C129	A2-B11-C130	A2-B11-C131	A2-B11-C132

A2-B11-C133	A2-B11-C134	A2-B11-C135	A2-B11-C136	A2-B11-C137	A2-B11-C138
A2-B11-C139	A2-B11-C140	BLANK	BLANK	BLANK	BLANK
A2-B12-C1	A2-B12-C2	A2-B12-C3	A2-B12-C4	A2-B12-C5	A2-B12-C6
A2-B12-C7	A2-B12-C8	A2-B12-C9	A2-B12-C10	A2-B12-C11	A2-B12-C12
A2-B12-C13	A2-B12-C14	A2-B12-C15	A2-B12-C16	A2-B12-C17	A2-B12-C18
A2-B12-C19	A2-B12-C20	A2-B12-C21	A2-B12-C22	A2-B12-C23	A2-B12-C24
A2-B12-C25	A2-B12-C26	A2-B12-C27	A2-B12-C28	A2-B12-C29	A2-B12-C30
A2-B12-C31	A2-B12-C32	A2-B12-C33	A2-B12-C34	A2-B12-C35	A2-B12-C36
A2-B12-C37	A2-B12-C38	A2-B12-C39	A2-B12-C40	A2-B12-C41	A2-B12-C42
A2-B12-C43	A2-B12-C44	A2-B12-C45	A2-B12-C46	A2-B12-C47	A2-B12-Ç48
A2-B12-C49	A2-B12-C50	A2-B12-C51	A2-B12-C52	A2-B12-C53	A2-B12-C54
A2-B12-C55	A2-B12-C56	A2-B12-C57	A2-B12-C58	A2-B12-C59	A2-B12-C60
A2-B12-C61	A2-B12-C62	A2-B12-C63	A2-B12-C64	A2-B12-C65	A2-B12-C66
A2-B12-C67	A2-B12-C68	A2-B12-C69	A2-B12-C70	A2-B12-C71	A2-B12-C72
A2-B12-C73	A2-B12-C74	A2-B12-C75	A2-B12-C76	A2-B12-C77	A2-B12-C78
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A2-B12-C85	A2-B12-C86	A2-B12-C87	A2-B12-C88	A2-B12-C89	A2-B12-C90
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A2-B12-C103	A2-B12-C104	A2-B12-C105	A2-B12-C106	A2-B12-C107	A2-B12-C108
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A2-B12-C127	A2-B12-C128	A2-B12-C129	A2-B12-C130	A2-B12-C131	A2-B12-C132
A2-B12-C133	A2-B12-C134	A2-B12-C135	A2-B12-C136	A2-B12-C137	A2-B12-C138
A2-B12-C139	A2-B12-C140	BLANK	BLANK	BLANK	BLANK
A2-B13-C1	A2-B13-C2	A2-B13-C3	A2-B13-C4	A2-B13-C5	A2-B13-C6
A2-B13-C7	A2-B13-C8	A2-B13-C9	A2-B13-C10	A2-B13-C11	A2-B13-C12
A2-B13-C13	A2-B13-C14	A2-B13-C15	A2-B13-C16	A2-B13-C17	A2-B13-C18
A2-B13-C19	A2-B13-C20	A2-B13-C21	A2-B13-C22	A2-B13-C23	A2-B13-C24
A2-B13-C25	A2-B13-C26	A2-B13-C27	A2-B13-C28	A2-B13-C29	A2-B13-C30
A2-B13-C31	A2-B13-C32	A2-B13-C33	A2-B13-C34	A2-B13-C35	A2-B13-C36
A2-B13-C37	A2-B13-C38	A2-B13-C39	A2-B13-C40	A2-B13-C41	A2-B13-C42
A2-B13-C43	A2-B13-C44	A2-B13-C45	A2-B13-C46	A2-B13-C47	A2-B13-C48
A2-B13-C49	A2-B13-C50	A2-B13-C51	A2-B13-C52	A2-B13-C53	A2-B13-C54
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	A2-B13-C79	A2-B13-C80	A2-B13-C81	A2-B13-C82	A2-B13-C83	A2-B13-C84
	A2-B13-C85	A2-B13-C86	A2-B13-C87	A2-B13-C88	A2-B13-C89	A2-B13-C90
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	A2-B13-C103	A2-B13-C104	A2-B13-C105	A2-B13-C106	A2-B13-C107	A2-B13-C108
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	A2-B13-C115	A2-B13-C116	A2-B13-C117	A2-B13-C118	A2-B13-C119	A2-B13-C120
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	A2-B13-C127	A2-B13-C128	A2-B13-C129	A2-B13-C130	A2-B13-C131	A2-B13-C132
	A2-B13-C133	A2-B13-C134	A2-B13-C135	A2-B13-C136	A2-B13-C137	A2-B13-C138
	A2-B13-C139	A2-B13-C140	BLANK	BLANK	BLANK	BLANK
	A3-B1-C1	A3-B1-C2	A3-B1-C3	A3-B1-C4	A3-B1-C5	A3-B1-C6
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	A3-B1-C13	A3-B1-C14	A3-B1-C15	A3-B1-C16	A3-B1-C17	A3-B1-C18
	A3-B1-C19	A3-B1-C20	A3-B1-C21	A3-B1-C22	A3-B1-C23	A3-B1-C24
	A3-B1-C25	A3-B1-C26	A3-B1-C27	A3-B1-C28	A3-B1-C29	A3-B1-C30
	A3-B1-C31	A3-B1-C32	A3-B1-C33	A3-B1-C34	A3-B1-C35	A3-B1-C36
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	A3-B1-C49	A3-B1-C50	A3-B1-C51	A3-B1-C52	A3-B1-C53	A3-B1-C54
	A3-B1-C55	A3-B1-C56	A3-B1-C57	A3-B1-C58	A3-B1-C59	A3-B1-C60
	A3-B1-C61	A3-B1-C62	A3-B1-C63	A3-B1-C64	A3-B1-C65	A3-B1-C66
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	A3-B1-C85	A3-B1-C86	A3-B1-C87	A3-B1-C88	A3-B1-C89	A3-B1-C90
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	A3-B1-C103	A3-B1-C104	A3-B1-C105	A3-B1-C106	A3-B1-C107	A3-B1-C108
	A3-B1-C109	A3-B1-C110	A3-B1-C111	A3-B1-C112	A3-B1-C113	A3-B1-C114
	A3-B1-C115	A3-B1-C116	A3-B1-C117	A3-B1-C118	A3-B1-C119	A3-B1-C120
	A3-B1-C121	A3-B1-C122	A3-B1-C123	A3-B1-C124	A3-B1-C125	A3-B1-C126
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	A3-B1-C133	A3-B1-C134	A3-B1-C135	A3-B1-C136	A3-B1-C137	A3-B1-C138
	A3-B1-C139	A3-B1-C140	BLANK	BLANK	BLANK	BLANK

	A3-B2-C1	A3-B2-C2	A3-B2-C3	A3-B2-C4	A3-B2-C5	A3-B2-C6
	A3-B2-C7	A3-B2-C8	A3-B2-C9	A3-B2-C10	A3-B2-C11	A3-B2-C12
	A3-B2-C13	A3-B2-C14	A3-B2-C15	A3-B2-C16	A3-B2-C17	A3-B2-C18
	A3-B2-C19	A3-B2-C20	A3-B2-C21	A3-B2-C22	A3-B2-C23	A3-B2-C24
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	A3-B2-C31	A3-B2-C32	A3-B2-C33	A3-B2-C34	A3-B2-C35	A3-B2-C36
	A3-B2-C37	A3-B2-C38	A3-B2-C39	- A3-B2-C40	A3-B2-C41	A3-B2-C42
	A3-B2-C43	A3-B2-C44	A3-B2-C45	A3-B2-C46	A3-B2-C47	A3-B2-C48
	A3-B2-C49	A3-B2-C50	A3-B2-C51	A3-B2-C52	A3-B2-C53	A3-B2-C54
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	A3-B2-C79	A3-B2-C80	A3-B2-C81	A3-B2-C82	A3-B2-C83	A3-B2-C84.
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	A3-B2-C103	A3-B2-C104	A3-B2-C105	A3-B2-C106	A3-B2-C107	A3-B2-C108
	A3-B2-C109	A3-B2-C110	A3-B2-C111	A3-B2-C112	A3-B2-C113	A3-B2-C114
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	A3-B2-C127	A3-B2-C128	A3-B2-C129	A3-B2-C130	A3-B2-C131	A3-B2-C132
	A3-B2-C133	A3-B2-C134	A3-B2-C135	A3-B2-C136	A3-B2-C137	A3-B2-C138
	A3-B2-C139	A3-B2-C140	BLANK	BLANK	BLANK	BLANK
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	A3-B3-C13	A3-B3-C14	A3-B3-C15	A3-B3-C16	A3-B3-C17	A3-B3-C18
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	A3-B3-C25	A3-B3-C26	A3-B3-C27	A3-B3-C28	A3-B3-C29	A3-B3-C30
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	A3-B3-C73	A3-B3-C74	A3-B3-C75	A3-B3-C76	A3-B3-C77	A3-B3-C78

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	A3-B3-C91	A3-B3-C92	A3-B3-C93	A3-B3-C94	A3-B3-C95	A3-B3-C96
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	A3-B3-C115	A3-B3-C116	A3-B3-C117	A3-B3-C118	A3-B3-C119	A3-B3-C120
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	A3-B4-C31	A3-B4-C32	A3-B4-C33	A3-B4-C34	A3-B4-C35	A3-B4-C36
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	A3-B4-C97	A3-B4-C98	A3-B4-C99	A3-B4-C100	A3-B4-C101	A3-B4-C102
	A3-B4-C103	A3-B4-C104	A3-B4-C105	A3-B4-C106	A3-B4-C107	A3-B4-C108
30	A3-B4-C109	A3-B4-C110	A3-B4-C111	A3-B4-C112	A3-B4-C113	A3-B4-C114
	A3-B4-C115	A3-B4-C116	A3-B4-C117	A3-B4-C118	A3-B4-C119	A3-B4-C120
	A3-B4-C121	A3-B4-C122	A3-B4-C123	A3-B4-C124	A3-B4-C125	A3-B4-C126
	A3-B4-C127	A3-B4-C128	A3-B4-C129	A3-B4-C130	A3-B4-C131	A3-B4-C132
	A3-B4-C133	A3-B4-C134	A3-B4-C135	A3-B4-C136	A3-B4-C137	A3-B4-C138
35	A3-B4-C139	A3-B4-C140	BLANK	BLANK	BLANK	BLANK
	A3-B5-C1	A3-B5-C2	A3-B5-C3	A3-B5-C4	A3-B5-C5	A3-B5-C6
	A3-B5-C7	A3-B5-C8	A3-B5-C9	A3-B5-C10	A3-B5-C11	A3-B5-C12
					-	

	A3-B5-C13	A3-B5-C14	A3-B5-C15	A3-B5-C16	A3-B5-C17	A3-B5-C18
	A3-B5-C19	A3-B5-C20	A3-B5-C21	A3-B5-C22	A3-B5-C23	A3-B5-C24
	A3-B5-C25	A3-B5-C26	A3-B5-C27	A3-B5-C28	A3-B5-C29	A3-B5-C30
	A3-B5-C31	A3-B5-C32	A3-B5-C33	A3-B5-C34	A3-B5-C35	A3-B5-C36
5	A3-B5-C37	A3-B5-C38	A3-B5-C39	A3-B5-C40	A3-B5-C41	A3-B5-C42
	A3-B5-C43	A3-B5-C44	A3-B5-C45	A3-B5-C46	A3-B5-C47	A3-B5-C48
	A3-B5-C49	A3-B5-C50	A3-B5-C51	A3-B5-C52	A3-B5-C53	A3-B5-C54
	A3-B5-C55	A3-B5-C56	A3-B5-C57	A3-B5-C58	A3-B5-C59	A3-B5-C60
	A3-B5-C61	A3-B5-C62	A3-B5-C63	A3-B5-C64	A3-B5-C65	A3-B5-C66
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	A3-B5-C73	A3-B5-C74	A3-B5-C75	A3-B5-C76	A3-B5-C77	A3-B5-C78
	A3-B5-C79	A3-B5-C80	A3-B5-C81	A3-B5-C82	A3-B5-C83	A3-B5-C84
	A3-B5-C85	A3-B5-C86	A3-B5-C87	A3-B5-C88	A3-B5-C89	A3-B5-C90
	A3-B5-C91	A3-B5-C92	A3-B5-C93	A3-B5-C94	A3-B5-C95	A3-B5-C96
15	A3-B5-C97	A3-B5-C98	A3-B5-C99	A3-B5-C100	A3-B5-C101	A3-B5-C102
	A3-B5-C103	A3-B5-C104	A3-B5-C105	A3-B5-C106	A3-B5-C107	A3-B5-C108
	A3-B5-C109	A3-B5-C110	A3-B5-C111	A3-B5-C112	A3-B5-C113	A3-B5-C114
	A3-B5-C115	A3-B5-C116	A3-B5-C117	A3-B5-C118	A3-B5-C119	A3-B5-C120
	A3-B5-C121	A3-B5-C122	A3-B5-C123	A3-B5-C124	A3-B5-C125	A3-B5-C126
20	A3-B5-C127	A3-B5-C128	A3-B5-C129	A3-B5-C130	A3-B5-C131	A3-B5-C132
	A3-B5-C133	A3-B5-C134	A3-B5-C135	A3-B5-C136	A3-B5-C137	A3-B5-C138
	A3-B5-C139	A3-B5-C140	BLANK	BLANK	BLANK	BLANK
	A3-B6-C1	A3-B6-C2	A3-B6-C3	A3-B6-C4	A3-B6-C5	A3-B6-C6
	A3-B6-C7	A3-B6-C8	A3-B6-C9	A3-B6-C10	A3-B6-C11	A3-B6-C12
25	A3-B6-C13	A3-B6-C14	A3-B6-C15	A3-B6-C16	A3-B6-C17	A3-B6-C18
	A3-B6-C19	A3-B6-C20	A3-B6-C21	A3-B6-C22	A3-B6-C23	A3-B6-C24
	A3-B6-C25	A3-B6-C26	A3-B6-C27	A3-B6-C28	A3-B6-C29	A3-B6-C30
	A3-B6-C31	A3-B6-C32	A3-B6-C33	A3-B6-C34	A3-B6-C35	A3-B6-C36
	A3-B6-C37	A3-B6-C38	A3-B6-C39	A3-B6-C40	A3-B6-C41	A3-B6-C42
30	A3-B6-C43	A3-B6-C44	A3-B6-C45	A3-B6-C46	A3-B6-C47	A3-B6-C48
	A3-B6-C49	A3-B6-C50	A3-B6-C51	A3-B6-C52	A3-B6-C53	A3-B6-C54
	A3-B6-C55	A3-B6-C56	A3-B6-C57	A3-B6-C58	A3-B6-C59	A3-B6-C60
	A3-B6-C61	A3-B6-C62	A3-B6-C63	A3-B6-C64	A3-B6-C65	A3-B6-C66
	A3-B6-C67	A3-B6-C68	A3-B6-C69	A3-B6-C70	A3-B6-C71	A3-B6-C72
35	A3-B6-C73	A3-B6-C74	A3-B6-C75	A3-B6-C76	A3-B6-C77	A3-B6-C78
	A3-B6-C79	A3-B6-C80	A3-B6-C81	A3-B6-C82	A3-B6-C83	A3-B6-C84
	A3-B6-C85	A3-B6-C86	A3-B6-C87	A3-B6-C88	A3-B6-C89	A3-B6-C90

	A3-B6-C91	A3-B6-C92	A3-B6-C93	A3-B6-C94	A3-B6-C95	A3-B6-C96
	A3-B6-C97	A3-B6-C98	A3-B6-C99	A3-B6-C100	A3-B6-C101	A3-B6-C102
	A3-B6-C103	A3-B6-C104	A3-B6-C105	A3-B6-C106	A3-B6-C107	A3-B6-C108
	A3-B6-C109	A3-B6-C110	A3-B6-C111	A3-B6-C112	A3-B6-C113	A3-B6-C114
5	A3-B6-C115	A3-B6-C116	A3-B6-C117	A3-B6-C118	A3-B6-C119	A3-B6-C120
	A3-B6-C121	A3-B6-C122	A3-B6-C123	A3-B6-C124	A3-B6-C125	A3-B6-C126
	A3-B6-C127	A3-B6-C128	A3-B6-C129	A3-B6-C130	A3-B6-C131	A3-B6-C132
	A3-B6-C133	A3-B6-C134	A3-B6-C135	A3-B6-C136	A3-B6-C137	A3-B6-C138
	A3-B6-C139	A3-B6-C140	BLANK	BLANK	BLANK	BLANK
10	A3-B7-C1	A3-B7-C2	A3-B7-C3	A3-B7-C4	A3-B7-C5	A3-B7-C6
	A3-B7-C7	A3-B7-C8	A3-B7-C9	A3-B7-C10	A3-B7-C11	A3-B7-C12
	A3-B7-C13	A3-B7-C14	A3-B7-C15	A3-B7-C16	A3-B7-C17	A3-B7-C18
	A3-B7-C19	A3-B7-C20	A3-B7-C21	A3-B7-C22	A3-B7-C23	A3-B7-C24
	A3-B7-C25	A3-B7-C26	A3-B7-C27	A3-B7-C28	A3-B7-C29	A3-B7-C30
15	A3-B7-C31	A3-B7-C32	A3-B7-C33	A3-B7-C34	A3-B7-C35	A3-B7-C36
	A3-B7-C37	A3-B7-C38	A3-B7-C39	A3-B7-C40	A3-B7-C41	A3-B7-C42
	A3-B7-C43	A3-B7-C44	A3-B7-C45	A3-B7-C46	A3-B7-C47	A3-B7-C48
	A3-B7-C49	A3-B7-C50	A3-B7-C51	A3-B7-C52	A3-B7-C53	A3-B7-C54
	A3-B7-C55	A3-B7-C56	A3-B7-C57	A3-B7-C58	A3-B7-C59	A3-B7-C60
20	A3-B7-C61	A3-B7-C62	A3-B7-C63	A3-B7-C64	A3-B7-C65	A3-B7-C66
	A3-B7-C67	A3-B7-C68	A3-B7-C69	A3-B7-C70	A3-B7-C71	A3-B7-C72
	A3-B7-C73	A3-B7-C74	A3-B7-C75	A3-B7-C76	A3-B7-C77	A3-B7-C78
	A3-B7-C79	A3-B7-C80	A3-B7-C81	A3-B7-C82	A3-B7-C83	A3-B7-C84
	A3-B7-C85	A3-B7-C86	A3-B7-C87	A3-B7-C88	A3-B7-C89	A3-B7-C90
25	A3-B7-C91	A3-B7-C92	A3-B7-C93	A3-B7-C94	A3-B7-C95	A3-B7-C96
	A3-B7-C97	A3-B7-C98	A3-B7-C99	A3-B7-C100	A3-B7-C101	A3-B7-C102
	A3-B7-C103	A3-B7-C104	A3-B7-C105	A3-B7-C106	A3-B7-C107	A3-B7-C108
	A3-B7-C109	A3-B7-C110	A3-B7-C111	A3-B7-C112	A3-B7-C113	A3-B7-C114
	A3-B7-C115	A3-B7-C116	A3-B7-C117	A3-B7-C118	A3-B7-C119	A3-B7-C120
30	A3-B7-C121	A3-B7-C122	A3-B7-C123	A3-B7-C124	A3-B7-C125	A3-B7-C126
	A3-B7-C127	A3-B7-C128	A3-B7-C129	A3-B7-C130	A3-B7-C131	A3-B7-C132
	A3-B7-C133	A3-B7-C134	A3-B7-C135	A3-B7-C136	A3-B7-C137	A3-B7-C138
	A3-B7-C139	A3-B7-C140	BLANK	BLANK	BLANK	BLANK
	A3-B8-C1	A3-B8-C2	A3-B8-C3	A3-B8-C4	A3-B8-C5	A3-B8-C6
35	A3-B8-C7	A3-B8-C8	A3-B8-C9	A3-B8-C10	A3-B8-C11	A3-B8-C12
	A3-B8-C13	A3-B8-C14	A3-B8-C15	A3-B8-C16	A3-B8-C17	A3-B8-C18
	A3-B8-C19	A3-B8-C20	A3-B8-C21	A3-B8-C22	A3-B8-C23	A3-B8-C24
						•

	A3-B8-C25	A3-B8-C26	A3-B8-C27	A3-B8-C28	A3-B8-C29	A3-B8-C30
	A3-B8-C31	A3-B8-C32	A3-B8-C33	A3-B8-C34	A3-B8-C35	A3-B8-C36
	A3-B8-C37	A3-B8-C38	A3-B8-C39	A3-B8-C40	A3-B8-C41	A3-B8-C42
	A3-B8-C43	A3-B8-C44	A3-B8-C45	A3-B8-C46	A3-B8-C47	A3-B8-C48
5	A3-B8-C49	A3-B8-C50	A3-B8-C51	A3-B8-C52	A3-B8-C53	A3-B8-C54
	A3-B8-C55	A3-B8-C56	A3-B8-C57	A3-B8-C58	A3-B8-C59	A3-B8-C60
	A3-B8-C61	A3-B8-C62	A3-B8-C63	A3-B8-C64	A3-B8-C65	A3-B8-C66
	A3-B8-C67	A3-B8-C68	A3-B8-C69	A3-B8-C70	A3-B8-C71	A3-B8-C72
	A3-B8-C73	A3-B8-C74	A3-B8-C75	A3-B8-C76	A3-B8-C77	A3-B8-C78
10	A3-B8-C79	A3-B8-C80	A3-B8-C81	A3-B8-C82	A3-B8-C83	A3-B8-C84
	A3-B8-C85	A3-B8-C86	A3-B8-C87	A3-B8-C88	A3-B8-C89	A3-B8-C90
	A3-B8-C91	A3-B8-C92	A3-B8-C93	A3-B8-C94	A3-B8-C95	A3-B8-C96
	A3-B8-C97	A3-B8-C98	A3-B8-C99	A3-B8-C100	A3-B8-C101	A3-B8-C102
	A3-B8-C103	A3-B8-C104	A3-B8-C105	A3-B8-C106	A3-B8-C107	A3-B8-C108
15	A3-B8-C109	A3-B8-C110	A3-B8-C111	A3-B8-C112	A3-B8-C113	A3-B8-C114
	A3-B8-C115	A3-B8-C116	A3-B8-C117	A3-B8-C118	A3-B8-C119	A3-B8-C120
	A3-B8-C121	A3-B8-C122	A3-B8-C123	A3-B8-C124	A3-B8-C125	A3-B8-C126
	A3-B8-C127	A3-B8-C128	A3-B8-C129	A3-B8-C130	A3-B8-C131	A3-B8-C132
	A3-B8-C133	A3-B8-C134	A3-B8-C135	A3-B8-C136	A3-B8-C137	A3-B8-C138
20	A3-B8-C139	A3-B8-C140	BLANK	BLANK	BLANK	BLANK
	A3-B9-C1	A3-B9-C2	A3-B9-C3	A3-B9-C4	A3-B9-C5	A3-B9-C6
	A3-B9-C7	A3-B9-C8	A3-B9-C9	A3-B9-C10	A3-B9-C11	A3-B9-C12
	A3-B9-C13	A3-B9-C14	A3-B9-C15	A3-B9-C16	A3-B9-C17	A3-B9-C18
	A3-B9-C19	A3-B9-C20	A3-B9-C21	A3-B9-C22	A3-B9-C23	A3-B9-C24
25	A3-B9-C25	A3-B9-C26	A3-B9-C27	A3-B9-C28	A3-B9-C29	A3-B9-C30
	A3-B9-C31	A3-B9-C32	A3-B9-C33	A3-B9-C34	A3-B9-C35	A3-B9-C36
	A3-B9-C37	A3-B9-C38	A3-B9-C39	A3-B9-C40	A3-B9-C41	A3-B9-C42
	A3-B9-C43	A3-B9-C44	A3-B9-C45	A3-B9-C46	A3-B9-C47	A3-B9-C48
	A3-B9-C49	A3-B9-C50	A3-B9-C51	A3-B9-C52	A3-B9-C53	A3-B9-C54
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	A3-B9-C61	A3-B9-C62	A3-B9-C63	A3-B9-C64	A3-B9-C65	A3-B9-C66
	A3-B9-C67	A3-B9-C68	A3-B9-C69	A3-B9-C70	A3-B9-C71	A3-B9-C72
	A3-B9-C73	A3-B9-C74	A3-B9-C75	A3-B9-C76	A3-B9-C77	A3-B9-C78
	A3-B9-C79	A3-B9-C80	A3-B9-C81	A3-B9-C82	A3-B9-C83	A3-B9-C84
35	A3-B9-C85	A3-B9-C86	A3-B9-C87	A3-B9-C88	A3-B9-C89	A3-B9-C90
	A3-B9-C91	A3-B9-C92	A3-B9-C93	A3-B9-C94	A3-B9-C95 '	A3-B9-C96
	A3-B9-C97	A3-B9-C98	A3-B9-C99	A3-B9-C100	A3-B9-C101	A3-B9-C102

	A3-B9-C103	A3-B9-C104	A3-B9-C105	A3-B9-C106	A3-B9-C107	A3-B9-C108
	A3-B9-C109	A3-B9-C110	A3-B9-C111	A3-B9-C112	A3-B9-C113	A3-B9-C114
	A3-B9-C115	A3-B9-C116	A3-B9-C117	A3-B9-C118	A3-B9-C119	A3-B9-C120
	A3-B9-C121	A3-B9-C122	A3-B9-C123	A3-B9-C124	A3-B9-C125	A3-B9-C126
5	A3-B9-C127	A3-B9-C128	A3-B9-C129	A3-B9-C130	A3-B9-C131	A3-B9-C132
	A3-B9-C133	A3-B9-C134	A3-B9-C135	A3-B9-C136	A3-B9-C137	A3-B9-C138
	A3-B9-C139	A3-B9-C140	BLANK	BLANK	BLANK	BLANK
	A3-B10-C1	A3-B10-C2	A3-B10-C3	A3-B10-C4	A3-B10-C5	A3-B10-C6
	A3-B10-C7	A3-B10-C8	A3-B10-C9	A3-B10-C10	A3-B10-C11	A3-B10-C12
10	A3-B10-C13	A3-B10-C14	A3-B10-C15	A3-B10-C16	A3-B10-C17	A3-B10-C18
	A3-B10-C19	A3-B10-C20	A3-B10-C21	A3-B10-C22	A3-B10-C23	A3-B10-C24
	A3-B10-C25	A3-B10-C26	A3-B10-C27	A3-B10-C28	A3-B10-C29	A3-B10-C30
	A3-B10-C31	A3-B10-C32	A3-B10-C33	A3-B10-C34	A3-B10-C35	A3-B10-C36
	A3-B10-C37	A3-B10-C38	A3-B10-C39	A3-B10-C40	A3-B10-C41	A3-B10-C42
15	A3-B10-C43	A3-B10-C44	A3-B10-C45	A3-B10-C46	A3-B10-C47	A3-B10-C48
	A3-B10-C49	A3-B10-C50	A3-B10-C51	A3-B10-C52	A3-B10-C53	A3-B10-C54
	A3-B10-C55	A3-B10-C56	A3-B10-C57	A3-B10-C58	A3-B10-C59	A3-B10-C60
	A3-B10-C61	A3-B10-C62	A3-B10-C63	A3-B10-C64.	A3-B10-C65	A3-B10-C66
	A3-B10-C67	A3-B10-C68	A3-B10-C69	A3-B10-C70	A3-B10-C71	A3-B10-C72
20	A3-B10-C73	A3-B10-C74	A3-B10-C75	A3-B10-C76	A3-B10-C77	A3-B10-C78
	A3-B10-C79	A3-B10-C80	A3-B10-C81	A3-B10-C82	A3-B10-C83	A3-B10-C84
	A3-B10-C85	A3-B10-C86	A3-B10-C87	A3-B10-C88	A3-B10-C89	A3-B10-C90
	A3-B10-C91	A3-B10-C92	A3-B10-C93	A3-B10-C94	A3-B10-C95	A3-B10-C96
	A3-B10-C97	A3-B10-C98	A3-B10-C99	A3-B10-C100	A3-B10-C101	A3-B10-C102
25	A3-B10-C103	A3-B10-C104	A3-B10-C105	A3-B10-C106	A3-B10-C107	A3-B10-C108
	A3-B10-C109	A3-B10-C110	A3-B10-C111	A3-B10-C112	A3-B10-C113	A3-B10-C114
	A3-B10-C115	A3-B10-C116	A3-B10-C117	A3-B10-C118	A3-B10-C119	A3-B10-C120
	A3-B10-C121	A3-B10-C122	A3-B10-C123	A3-B10-C124	A3-B10-C125	A3-B10-C126
	A3-B10-C127	A3-B10-C128	A3-B10-C129	A3-B10-C130	A3-B10-C131	A3-B10-C132
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	A3-B10-C139	A3-B10-C140	BLANK	BLANK	BLANK	BLANK
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	A3-B11-C7	A3-B11-C8	A3-B11-C9	A3-B11-C10	A3-B11-C11	A3-B11-C12
	A3-B11-C13	A3-B11-C14	A3-B11-C15	A3-B11-C16	A3-B11-C17	A3-B11-C18
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	A3-B11-C31	A3-B11-C32	A3-B11-C33	A3-B11-C34	A3-B11-C35	A3-B11-C36

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A3-B11-C133	A3-B11-C134	A3-B11-C135	A3-B11-C136	A3-B11-C137	A3-B11-C138
A3-B11-C139	A3-B11-C140	BLANK	BLANK	BLANK	BLANK
A3-B12-C1	A3-B12-C2	A3-B12-C3	A3-B12-C4	A3-B12-C5	A3-B12-C6
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	A3-B12-C127	A3-B12-C128	A3-B12-C129	A3-B12-C130	A3-B12-C131	A3-B12-C132
	A3-B12-C133	A3-B12-C134	A3-B12-C135	A3-B12-C136	A3-B12-C137	A3-B12-C138
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	A3-B13-C1	A3-B13-C2	A3-B13-C3	A3-B13-C4	A3-B13-C5	A3-B13-C6
	A3-B13-C7	A3-B13-C8	A3-B13-C9	A3-B13-C10	A3-B13-C11	A3-B13-C12
	A3-B13-C13	A3-B13-C14	A3-B13-C15	A3-B13-C16	A3-B13-C17	A3-B13-C18
	A3-B13-C19	A3-B13-C20	A3-B13-C21	A3-B13-C22	A3-B13-C23	A3-B13-C24
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	A3-B13-C31	A3-B13-C32	A3-B13-C33	A3-B13-C34	A3-B13-C35	A3-B13-C36
	A3-B13-C37	A3-B13-C38	A3-B13-C39	A3-B13-C40	A3-B13-C41	A3-B13-C42
	A3-B13-C43	A3-B13-C44	A3-B13-C45	A3-B13-C46	A3-B13-C47	A3-B13-C48
	A3-B13-C49	A3-B13-C50	A3-B13-C51	A3-B13-C52	A3-B13-C53	A3-B13-C54
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	A3-B13-C103	A3-B13-C104	A3-B13-C105	A3-B13-C106	A3-B13-C107	A3-B13-C108
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	A3-B13-C133	A3-B13-C134	A3-B13-C135	A3-B13-C136	A3-B13-C137	A3-B13-C138
	A3-B13-C139	A3-B13-C140	BLANK	BLANK	BLANK	BLANK
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	A4-B1-C7	A4-B1-C8	A4-B1-C9	A4-B1-C10	A4-B1-C11	A4-B1-C12
	A4-B1-C13	A4-B1-C14	A4-B1-C15	A4-B1-C16	A4-B1-C17	A4-B1-C18
	A4-B1-C19	A4-B1-C20	A4-B1-C21	A4-B1-C22	A4-B1-C23	A4-B1-C24
	A4-B1-C25	A4-B1-C26	A4-B1-C27	A4-B1-C28	A4-B1-C29	A4-B1-C30
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	A4-B1-C37	A4-B1-C38	A4-B1-C39	A4-B1-C40	A4-B1-C41	A4-B1-C42
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	A4-B1-C85	A4-B1-C86	A4-B1-C87	A4-B1-C88	A4-B1-C89	A4-B1-C90
	A4-B1-C91	A4-B1-C92	A4-B1-C93	A4-B1-C94	A4-B1-C95	A4-B1-C96
	A4-B1-C97	A4-B1-C98	A4-B1-C99	A4-B1-C100	A4-B1-C101	A4-B1-C102
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	A4-B1-C109	A4-B1-C110	A4-B1-C111	A4-B1-C112	A4-B1-C113	A4-B1-C114
	A4-B1-C115	A4-B1-C116	A4-B1-C117	A4-B1-C118	A4-B1-C119	A4-B1-C120
	A4-B1-C121	A4-B1-C122	A4-B1-C123	A4-B1-C124	A4-B1-C125	A4-B1-C126
	A4-B1-C127	A4-B1-C128	A4-B1-C129	A4-B1-C130	A4-B1-C131	A4-B1-C132
15	A4-B1-C133	A4-B1-C134	A4-B1-C135	A4-B1-C136	A4-B1-C137	A4-B1-C138
	A4-B1-C139	A4-B1-C140	BLANK	BLANK	BLANK	BLANK
	A4-B2-C1	A4-B2-C2	A4-B2-C3	A4-B2-C4	A4-B2-C5	A4-B2-C6
	A4-B2-C7	A4-B2-C8	A4-B2-C9	A4-B2-C10	A4-B2-C11	A4-B2-C12
	A4-B2-C13	A4-B2-C14	A4-B2-C15	A4-B2-C16	A4-B2-C17	A4-B2-C18
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	A4-B2-C25	A4-B2-C26	A4-B2-C27	A4-B2-C28	A4-B2-C29	A4-B2-C30
	A4-B2-C31	A4-B2-C32	A4-B2-C33	A4-B2-C34	A4-B2-C35	A4-B2-C36
	A4-B2-C37	A4-B2-C38	A4-B2-C39	A4-B2-C40	A4-B2-C41	A4-B2-C42
	A4-B2-C43	A4-B2-C44	A4-B2-C45	A4-B2-C46	A4-B2-C47	A4-B2-C48
25	A4-B2-C49	A4-B2-C50	A4-B2-C51	A4-B2-C52	A4-B2-C53	A4-B2-C54
	A4-B2-C55	A4-B2-C56	A4-B2-C57	A4-B2-C58	A4-B2-C59	A4-B2-C60
	A4-B2-C61	A4-B2-C62	A4-B2-C63	A4-B2-C64	A4-B2-C65	A4-B2-C66
	A4-B2-C67	A4-B2-C68	A4-B2-C69	A4-B2-C70	A4-B2-C71	A4-B2-C72
	A4-B2-C73	A4-B2-C74	A4-B2-C75	A4-B2-C76	A4-B2-C77	A4-B2-C78
30	A4-B2-C79	A4-B2-C80	A4-B2-C81	A4-B2-C82	A4-B2-C83	A4-B2-C84
	A4-B2-C85	A4-B2-C86	A4-B2-C87	A4-B2-C88	A4-B2-C89	A4-B2-C90
	A4-B2-C91	A4-B2-C92	A4-B2-C93	A4-B2-C94	A4-B2-C95	A4-B2-C96
	A4-B2-C97	A4-B2-C98	A4-B2-C99	A4-B2-C100	A4-B2-C101	A4-B2-C102
	A4-B2-C103	A4-B2-C104	A4-B2-C105	A4-B2-C106	A4-B2-C107	A4-B2-C108
35	A4-B2-C109	A4-B2-C110	A4-B2-C111	A4-B2-C112	A4-B2-C113	A4-B2-C114
	A4-B2-C115	A4-B2-C116	A4-B2-C117	A4-B2-C118	A4-B2-C119	A4-B2-C120
	A4-B2-C121	A4-B2-C122	A4-B2-C123	A4-B2-C124	A4-B2-C125	A4-B2-C126

	A4-B2-C127	A4-B2-C128	A4-B2-C129	A4-B2-C130	A4-B2-C131	A4-B2-C132
	A4-B2-C133	A4-B2-C134	A4-B2-C135	A4-B2-C136	A4-B2-C137	A4-B2-C138
	A4-B2-C139	A4-B2-C140	BLANK	BLANK	BLANK	BLANK
	A4-B3-C1	A4-B3-C2	A4-B3-C3	A4-B3-C4	A4-B3-C5	A4-B3-C6
5	A4-B3-C7	A4-B3-C8	A4-B3-C9	A4-B3-C10	A4-B3-C11	A4-B3-C12
	A4-B3-C13	A4-B3-C14	A4-B3-C15	A4-B3-C16	A4-B3-C17	A4-B3-C18
	A4-B3-C19	A4-B3-C20	A4-B3-C21	A4-B3-C22	A4-B3-C23	A4-B3-C24
	A4-B3-C25	A4-B3-C26	A4-B3-C27	A4-B3-C28	A4-B3-C29	A4-B3-C30
	A4-B3-C31	A4-B3-C32	A4-B3-C33	A4-B3-C34	A4-B3-C35	A4-B3-C36
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-	A4-B3-C43	A4-B3-C44	A4-B3-C45	A4-B3-C46	A4-B3-C47	A4-B3-C48
	A4-B3-C49	A4-B3-C50	A4-B3-C51	A4-B3-C52	A4-B3-C53	A4-B3-C54
	A4-B3-C55	A4-B3-C56	A4-B3-C57	A4-B3-C58	A4-B3-C59	A4-B3-C60
	A4-B3-C61	A4-B3-C62	A4-B3-C63	A4-B3-C64	A4-B3-C65	A4-B3-C66
15	A4-B3-C67	A4-B3-C68	A4-B3-C69	A4-B3-C70	A4-B3-C71	A4-B3-C72
	A4-B3-C73	A4-B3-C74	A4-B3-C75	A4-B3-C76	A4-B3-C77	A4-B3-C78
	A4-B3-C79	A4-B3-C80	A4-B3-C81	A4-B3-C82	A4-B3-C83	A4-B3-C84
	A4-B3-C85	A4-B3-C86	A4-B3-C87	A4-B3-C88	A4-B3-C89	A4-B3-C90
	A4-B3-C91	A4-B3-C92	A4-B3-C93	A4-B3-C94	A4-B3-C95	A4-B3-C96
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	A4-B3-C103	A4-B3-C104	A4-B3-C105	A4-B3-C106	A4-B3-C107	A4-B3-C108
	A4-B3-C109	A4-B3-C110	A4-B3-C111	A4-B3-C112	A4-B3-C113	A4-B3-C114
	A4-B3-C115	A4-B3-C116	A4-B3-C117	A4-B3-C118	A4-B3-C119	A4-B3-C120
	A4-B3-C121	A4-B3-C122	A4-B3-C123	A4-B3-C124	A4-B3-C125	A4-B3-C126
25	A4-B3-C127	A4-B3-C128	A4-B3-C129	A4-B3-C130	A4-B3-C131	A4-B3-C132
	A4-B3-C133	A4-B3-C134	A4-B3-C135	A4-B3-C136	A4-B3-C137	A4-B3-C138
	A4-B3-C139	A4-B3-C140	BLANK	BLANK	BLANK	BLANK
	A4-B4-C1	A4-B4-C2	A4-B4-C3	A4-B4-C4	A4-B4-C5	A4-B4-C6
	A4-B4-C7	A4-B4-C8	A4-B4-C9	A4-B4-C10	A4-B4-C11	A4-B4-C12
30	A4-B4-C13	A4-B4-C14	A4-B4-C15	A4-B4-C16	A4-B4-C17	A4-B4-C18
	A4-B4-C19	A4-B4-C20	A4-B4-C21	A4-B4-C22	A4-B4-C23	A4-B4-C24
	A4-B4-C25	A4-B4-C26	A4-B4-C27	A4-B4-C28	A4-B4-C29	A4-B4-C30
	A4-B4-C31	A4-B4-C32	A4-B4-C33	A4-B4-C34	A4-B4-C35	A4-B4-C36
	A4-B4-C37	A4-B4-C38	A4-B4-C39	A4-B4-C40	A4-B4-C41	A4-B4-C42
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	A4-B4-C49	A4-B4-C50	A4-B4-C51	A4-B4-C52	A4-B4-C53	A4-B4-C54
	A4-B4-C55	A4-B4-C56	A4-B4-C57	A4-B4-C58	A4-B4-C59	A4-B4-C60

	A4-B4-C61	A4-B4-C62	A4-B4-C63	A4-B4-C64	A4-B4-C65	A4-B4-C66
	A4-B4-C67	A4-B4-C68	A4-B4-C69	A4-B4-C70	A4-B4-C71	A4-B4-C72
	A4-B4-C73	A4-B4-C74	A4-B4-C75	A4-B4-C76	A4-B4-C77	A4-B4-C78
	A4-B4-C79	A4-B4-C80	A4-B4-C81	A4-B4-C82	A4-B4-C83	A4-B4-C84
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	A4-B4-C97	A4-B4-C98	A4-B4-C99	A4-B4-C100	A4-B4-C101	A4-B4-C102
	A4-B4-C103	A4-B4-C104	A4-B4-C105	A4-B4-C106	A4-B4-C107	A4-B4-C108
	A4-B4-C109	A4-B4-C110	A4-B4-C111	A4-B4-C112	A4-B4-C113	A4-B4-C114
10	A4-B4-C115	A4-B4-C116	A4-B4-C117	A4-B4-C118	A4-B4-C119	A4-B4-C120
	A4-B4-C121	A4-B4-C122	A4-B4-C123	A4-B4-C124	A4-B4-C125	A4-B4-C126
	A4-B4-C127	A4-B4-C128	A4-B4-C129	A4-B4-C130	A4-B4-C131	A4-B4-C132
	A4-B4-C133	A4-B4-C134	A4-B4-C135	A4-B4-C136	A4-B4-C137	A4-B4-C138
	A4-B4-C139	A4-B4-C140	BLANK	BLANK	BLANK	BLANK
15	A4-B5-C1	A4-B5-C2	A4-B5-C3	A4-B5-C4	A4-B5-C5	A4-B5-C6
	A4-B5-C7	A4-B5-C8	A4-B5-C9	A4-B5-C10	A4-B5-C11	A4-B5-C12
	A4-B5-C13	A4-B5-C14	A4-B5-C15	A4-B5-C16	A4-B5-C17	A4-B5-C18
	A4-B5-C19	A4-B5-C20	A4-B5-C21	A4-B5-C22	A4-B5-C23	A4-B5-C24
	A4-B5-C25	A4-B5-C26	A4-B5-C27	A4-B5-C28	A4-B5-C29	A4-B5-C30
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	A4-B5-C37	A4-B5-C38	A4-B5-C39	A4-B5-C40	A4-B5-C41	A4-B5-C42
	A4-B5-C43	A4-B5-C44	A4-B5-C45	A4-B5-C46	A4-B5-C47	A4-B5-C48
	A4-B5-C49	A4-B5-C50	A4-B5-C51	A4-B5-C52	A4-B5-C53	A4-B5-C54
	A4-B5-C55	A4-B5-C56	A4-B5-C57	A4-B5-C58	A4-B5-C59	A4-B5-C60
25	A4-B5-C61	A4-B5-C62	A4-B5-C63	A4-B5-C64	A4-B5-C65	A4-B5-C66
	A4-B5-C67	A4-B5-C68	A4-B5-C69	A4-B5-C70	A4-B5-C71	A4-B5-C72
	A4-B5-C73	A4-B5-C74	A4-B5-C75	A4-B5-C76	A4-B5-C77	A4-B5-C78
	A4-B5-C79	A4-B5-C80	A4-B5-C81	A4-B5-C82	A4-B5-C83	A4-B5-C84
•	A4-B5-C85	A4-B5-C86	A4-B5-C87	A4-B5-C88	A4-B5-C89	A4-B5-C90
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	A4-B5-C97	A4-B5-C98	A4-B5-C99	A4-B5-C100	A4-B5-C101	A4-B5-C102
	A4-B5-C103	A4-B5-C104	A4-B5-C105	A4-B5-C106	A4-B5-C107	A4-B5-C108
	A4-B5-C109	A4-B5-C110	A4-B5-C111	A4-B5-C112	A4-B5-C113	A4-B5-C114
	A4-B5-C115	A4-B5-C116	A4-B5-C117	A4-B5-C118	A4-B5-C119	A4-B5-C120
35	A4-B5-C121	A4-B5-C122	A4-B5-C123	A4-B5-C124	A4-B5-C125	A4-B5-C126
	A4-B5-C127	A4-B5-C128	A4-B5-C129	A4-B5-C130	A4-B5-C131	A4-B5-C132
	A4-B5-C133	A4-B5-C134	A4-B5-C135	A4-B5-C136	A4-B5-C137	A4-B5-C138

	A4-B5-C139	A4-B5-C140	BLANK	BLANK	BLANK	BLANK
	A4-B6-C1	A4-B6-C2	A4-B6-C3	A4-B6-C4	A4-B6-C5	A4-B6-C6
	A4-B6-C7	A4-B6-C8	A4-B6-C9	A4-B6-C10	A4-B6-C11	A4-B6-C12
	A4-B6-C13	A4-B6-C14	A4-B6-C15	A4-B6-C16	A4-B6-C17	A4-B6-C18
5	A4-B6-C19	A4-B6-C20	A4-B6-C21	A4-B6-C22	A4-B6-C23	A4-B6-C24
	A4-B6-C25	A4-B6-C26	A4-B6-C27	A4-B6-C28	A4-B6-C29	A4-B6-C30
	A4-B6-C31	A4-B6-C32	A4-B6-C33	A4-B6-C34	A4-B6-C35	A4-B6-C36
	A4-B6-C37	A4-B6-C38	A4-B6-C39	A4-B6-C40	A4-B6-C41	A4-B6-C42
	A4-B6-C43	A4-B6-C44	A4-B6-C45	A4-B6-C46	A4-B6-C47	A4-B6-C48
10	A4-B6-C49	A4-B6-C50	A4-B6-C51	A4-B6-C52	A4-B6-C53	A4-B6-C54
	A4-B6-C55	A4-B6-C56	A4-B6-C57	A4-B6-C58	A4-B6-C59	A4-B6-C60
	A4-B6-C61	A4-B6-C62	A4-B6-C63	A4-B6-C64	A4-B6-C65	A4-B6-C66
	A4-B6-C67	A4-B6-C68	A4-B6-C69	A4-B6-C70	A4-B6-C71	A4-B6-C72
	A4-B6-C73	A4-B6-C74	A4-B6-C75	A4-B6-C76	A4-B6-C77	A4-B6-C78
15	A4-B6-C79	A4-B6-C80	A4-B6-C81	A4-B6-C82	A4-B6-C83	A4-B6-C84
	A4-B6-C85	A4-B6-C86	A4-B6-C87	A4-B6-C88	A4-B6-C89	A4-B6-C90
	A4-B6-C91	A4-B6-C92	A4-B6-C93	A4-B6-C94	A4-B6-C95	A4-B6-C96
-	A4-B6-C97	A4-B6-C98	A4-B6-C99	A4-B6-C100	A4-B6-C101	A4-B6-C102
	A4-B6-C103	A4-B6-C104	A4-B6-C105	A4-B6-C106	A4-B6-C107	A4-B6-C108
20	A4-B6-C109	A4-B6-C110	A4-B6-C111	A4-B6-C112	A4-B6-C113	A4-B6-C114
	A4-B6-C115	A4-B6-C116	A4-B6-C117	A4-B6-C118	A4-B6-C119	A4-B6-C120
	A4-B6-C121	A4-B6-C122	A4-B6-C123	A4-B6-C124	A4-B6-C125	A4-B6-C126
	A4-B6-C127	A4-B6-C128	A4-B6-C129	A4-B6-C130	A4-B6-C131	A4-B6-C132
	A4-B6-C133	A4-B6-C134	A4-B6-C135	A4-B6-C136	A4-B6-C137	A4-B6-C138
25	A4-B6-C139	A4-B6-C140	BLANK	BLANK	BLANK	BLANK
	A4-B7-C1	A4-B7-C2	A4-B7-C3	A4-B7-C4	A4-B7-C5	A4-B7-C6
	A4-B7-C7	A4-B7-C8	A4-B7-C9	A4-B7-C10	A4-B7-C11	A4-B7-C12
	A4-B7-C13	A4-B7-C14	A4-B7-C15	A4-B7-C16	A4-B7-C17	A4-B7-C18
	A4-B7-C19	A4-B7-C20	A4-B7-C21	A4-B7-C22	A4-B7-C23	A4-B7-C24
30	A4-B7-C25	A4-B7-C26	A4-B7-C27	A4-B7-C28	A4-B7-C29	A4-B7-C30
	A4-B7-C31	A4-B7-C32	A4-B7-C33	A4-B7-C34	A4-B7-C35	A4-B7-C36
	A4-B7-C37	A4-B7-C38	A4-B7-C39	A4-B7-C40	A4-B7-C41	A4-B7-C42
	A4-B7-C43	A4-B7-C44	A4-B7-C45	A4-B7-C46	A4-B7-C47	A4-B7-C48
	A4-B7-C49	A4-B7-C50	A4-B7-C51	A4-B7-C52	A4-B7-C53	A4-B7-C54
35	A4-B7-C55	A4-B7-C56	A4-B7-C57	A4-B7-C58	A4-B7-C59	A4-B7-C60
	A4-B7-C61	A4-B7-C62	A4-B7-C63	A4-B7-C64	A4-B7-C65	A4-B7-C66
	A4-B7-C67	A4-B7-C68	A4-B7-C69	A4-B7-C70	A4-B7-C71	A4-B7-C72

	A4-B7-C73	A4-B7-C74	A4-B7-C75	A4-B7-C76	A4-B7-C77	A4-B7-C78
	A4-B7-C79	A4-B7-C80	A4-B7-C81	A4-B7-C82	A4-B7-C83	A4-B7-C84
	A4-B7-C85	A4-B7-C86	A4-B7-C87	A4-B7-C88	A4-B7-C89	A4-B7-C90
	A4-B7-C91	A4-B7-C92	A4-B7-C93	A4-B7-C94	A4-B7-C95	A4-B7-C96
5	A4-B7-C97	A4-B7-C98	A4-B7-C99	A4-B7-C100	A4-B7-C101	A4-B7-C102
	A4-B7-C103	A4-B7-C104	A4-B7-C105	A4-B7-C106	A4-B7-C107	A4-B7-C108
	A4-B7-C109	A4-B7-C110	A4-B7-C111	A4-B7-C112	A4-B7-C113	A4-B7-C114
	A4-B7-C115	A4-B7-C116	·A4-B7-C117	A4-B7-C118	A4-B7-C119	A4-B7-C120
	A4-B7-C121	A4-B7-C122	A4-B7-C123	A4-B7-C124	A4-B7-C125	A4-B7-C126
10	A4-B7-C127	A4-B7-C128	A4-B7-C129	A4-B7-C130	A4-B7-C131	A4-B7-C132
	A4-B7-C133	A4-B7-C134	A4-B7-C135	A4-B7-C136	A4-B7-C137	A4-B7-C138
	A4-B7-C139	A4-B7-C140	BLANK	BLANK	BLANK	BLANK
	A4-B8-C1	A4-B8-C2	A4-B8-C3	A4-B8-C4	A4-B8-C5	A4-B8-C6
	A4-B8-C7	A4-B8-C8	A4-B8-C9	A4-B8-C10	A4-B8-C11	A4-B8-C12
15	A4-B8-C13	A4-B8-C14	A4-B8-C15	A4-B8-C16	A4-B8-C17	A4-B8-C18
	A4-B8-C19	A4-B8-C20	A4-B8-C21	A4-B8-C22	A4-B8-C23	A4-B8-C24
	A4-B8-C25	A4-B8-C26	A4-B8-C27	A4-B8-C28	A4-B8-C29	A4-B8-C30
	A4-B8-C31	A4-B8-C32	A4-B8-C33	A4-B8-C34	A4-B8-C35	A4-B8-C36
	A4-B8-C37	A4-B8-C38	A4-B8-C39	A4-B8-C40	A4-B8-C41	A4-B8-C42
20	A4-B8-C43	A4-B8-C44	A4-B8-C45	A4-B8-C46	A4-B8-C47	A4-B8-C48
	A4-B8-C49	A4-B8-C50	A4-B8-C51	A4-B8-C52	A4-B8-C53	A4-B8-C54
	A4-B8-C55	A4-B8-C56	A4-B8-C57	A4-B8-C58	A4-B8-C59	A4-B8-C60
	A4-B8-C61	A4-B8-C62	A4-B8-C63	A4-B8-C64	A4-B8-C65	A4-B8-C66
	A4-B8-C67	A4-B8-C68	A4-B8-C69	A4-B8-C70	A4-B8-C71	A4-B8-C72
25	A4-B8-C73	A4-B8-C74	A4-B8-C75	A4-B8-C76	A4-B8-C77	A4-B8-C78
	A4-B8-C79	A4-B8-C80	A4-B8-C81	A4-B8-C82	A4-B8-C83	A4-B8-C84
	A4-B8-C85	A4-B8-C86	A4-B8-C87	A4-B8-C88	A4-B8-C89	A4-B8-C90
	A4-B8-C91	A4-B8-C92	A4-B8-C93	A4-B8-C94	A4-B8-C95	A4-B8-C96
	A4-B8-C97	A4-B8-C98	A4-B8-C99	A4-B8-C100	A4-B8-C101	A4-B8-C102
30	A4-B8-C103	A4-B8-C104	A4-B8-C105	A4-B8-C106	A4-B8-C107	A4-B8-C108
	A4-B8-C109	A4-B8-C110	A4-B8-C111	A4-B8-C112	A4-B8-C113	A4-B8-C114
	A4-B8-C115	A4-B8-C116	A4-B8-C117	A4-B8-C118	A4-B8-C119	A4-B8-C120
•	A4-B8-C121	A4-B8-C122	A4-B8-C123	A4-B8-C124	A4-B8-C125	A4-B8-C126
	A4-B8-C127	A4-B8-C128	A4-B8-C129	A4-B8-C130	A4-B8-C131	A4-B8-C132
35	A4-B8-C133	A4-B8-C134	A4-B8-C135	A4-B8-C136	A4-B8-C137	A4-B8-C138
	A4-B8-C139	A4-B8-C140	BLANK	BLANK	BLANK	BLANK
	A4-B9-C1	A4-B9-C2	A4-B9-C3	A4-B9-C4	A4-B9-C5	A4-B9-C6

	A4-B9-C7	A4-B9-C8	A4-B9-C9	A4-B9-C10	A4-B9-C11	A4-B9-C12
	A4-B9-C13	A4-B9-C14	A4-B9-C15	A4-B9-C16	A4-B9-C17	A4-B9-C18
	A4-B9-C19	A4-B9-C20	A4-B9-C21	A4-B9-C22	A4-B9-C23	A4-B9-C24
	A4-B9-C25	A4-B9-C26	A4-B9-C27	A4-B9-C28	A4-B9-C29	A4-B9-C30
5	A4-B9-C31	A4-B9-C32	A4-B9-C33	A4-B9-C34	A4-B9-C35	A4-B9-C36
	A4-B9-C37	A4-B9-C38	A4-B9-C39	A4-B9-C40	A4-B9-C41	A4-B9-C42
	A4-B9-C43	A4-B9-C44	A4-B9-C45	A4-B9-C46	A4-B9-C47	A4-B9-C48
	A4-B9-C49	A4-B9-C50	A4-B9-C51	A4-B9-C52	A4-B9-C53	A4-B9-C54
	A4-B9-C55	A4-B9-C56	A4-B9-C57	A4-B9-C58	A4-B9-C59	A4-B9-C60
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	A4-B9-C67	A4-B9-C68	A4-B9-C69	A4-B9-C70	A4-B9-C71	A4-B9-C72
	A4-B9-C73	A4-B9-C74	A4-B9-C75	A4-B9-C76	A4-B9-C77	A4-B9-C78
	A4-B9-C79	A4-B9-C80	A4-B9-C81	A4-B9-C82	A4-B9-C83	A4-B9-C84
	A4-B9-C85	A4-B9-C86	A4-B9-C87	A4-B9-C88	A4-B9-C89	A4-B9-C90
15	A4-B9-C91	A4-B9-C92	A4-B9-C93	A4-B9-C94	A4-B9-C95	A4-B9-C96
	A4-B9-C97	A4-B9-C98	A4-B9-C99	A4-B9-C100	A4-B9-C101	A4-B9-C102
	A4-B9-C103	A4-B9-C104	A4-B9-C105	A4-B9-C106	A4-B9-C107	A4-B9-C108
	A4-B9-C109	A4-B9-C110	A4-B9-C111	A4-B9-C112	A4-B9-C113	A4-B9-C114
	A4-B9-C115	A4-B9-C116	A4-B9-C117	A4-B9-C118	A4-B9-C119	A4-B9-C120
20	A4-B9-C121	A4-B9-C122	A4-B9-C123	A4-B9-C124	A4-B9-C125	A4-B9-C126
	A4-B9-C127	A4-B9-C128	A4-B9-C129	A4-B9-C130	A4-B9-C131	A4-B9-C132
	A4-B9-C133	A4-B9-C134	A4-B9-C135	A4-B9-C136	A4-B9-C137	A4-B9-C138
	A4-B9-C139	A4-B9-C140	BLANK	BLANK	BLANK	BLANK
	A4-B10-C1	A4-B10-C2	A4-B10-C3	A4-B10-C4	A4-B10-C5	A4-B10-C6
25	A4-B10-C7	A4-B10-C8	A4-B10-C9	A4-B10-C10	A4-B10-C11	A4-B10-C12
	A4-B10-C13	A4-B10-C14	A4-B10-C15	A4-B10-C16	A4-B10-C17	A4-B10-C18
	A4-B10-C19	A4-B10-C20	A4-B10-C21	A4-B10-C22	A4-B10-C23	A4-B10-C24
	A4-B10-C25	A4-B10-C26	A4-B10-C27	A4-B10-C28	A4-B10-C29	A4-B10-C30
	A4-B10-C31	A4-B10-C32	A4-B10-C33	A4-B10-C34	A4-B10-C35	A4-B10-C36
30	A4-B10-C37	A4-B10-C38	A4-B10-C39	A4-B10-C40	A4-B10-C41	A4-B10-C42
	A4-B10-C43	A4-B10-C44	A4-B10-C45	A4-B10-C46	A4-B10-C47	A4-B10-C48
	A4-B10-C49	A4-B10-C50	A4-B10-C51	A4-B10-C52	A4-B10-C53	A4-B10-C54
	A4-B10-C55	A4-B10-C56	A4-B10-C57	A4-B10-C58	A4-B10-C59	A4-B10-C60
	A4-B10-C61	A4-B10-C62	A4-B10-C63	A4-B10-C64	A4-B10-C65	A4-B10-C66
3 <i>5</i>	A4-B10-C67	A4-B10-C68	A4-B10-C69	A4-B10-C70	A4-B10-C71	A4-B10-C72
	A4-B10-C73	A4-B10-C74	A4-B10-C75	A4-B10-C76	A4-B10-C77	A4-B10-C78
	A4-B10-C79	A4-B10-C80	A4-B10-C81	A4-B10-C82	A4-B10-C83	A4-B10-C84

	A4-B10-C85	A4-B10-C86	A4-B10-C87	A4-B10-C88	A4-B10-C89	A4-B10-C90
	A4-B10-C91	A4-B10-C92	A4-B10-C93	A4-B10-C94	A4-B10-C95	A4-B10-C96
	A4-B10-C97	A4-B10-C98	A4-B10-C99	A4-B10-C100	A4-B10-C101	A4-B10-C102
	A4-B10-C103	A4-B10-C104	A4-B10-C105	A4-B10-C106	A4-B10-C107	A4-B10-C108
5	A4-B10-C109	A4-B10-C110	A4-B10-C111	A4-B10-C112	A4-B10-C113	A4-B10-C114
	A4-B10-C115	A4-B10-C116	A4-B10-C117	A4-B10-C118	A4-B10-C119	A4-B10-C120
	A4-B10-C121	A4-B10-C122	A4-B10-C123	A4-B10-C124	A4-B10-C125	A4-B10-C126
	A4-B10-C127	A4-B10-C128	A4-B10-C129	A4-B10-C130	A4-B10-C131	A4-B10-C132
	A4-B10-C133	A4-B10-C134	A4-B10-C135	A4-B10-C136	A4-B10-C137	A4-B10-C138
10	A4-B10-C139	A4-B10-C140	BLANK	BLANK	BLANK	BLANK
	A4-B11-C1	A4-B11-C2	A4-B11-C3	A4-B11-C4	A4-B11-C5	A4-B11-C6
	A4-B11-C7	A4-B11-C8	A4-B11-C9	A4-B11-C10	A4-B11-C11	A4-B11-C12
	A4-B11-C13	A4-B11-C14	A4-B11-C15	A4-B11-C16	A4-B11-C17	A4-B11-C18
	A4-B11-C19	A4-B11-C20	A4-B11-C21	A4-B11-C22	A4-B11-C23	A4-B11-C24
15	A4-B11-C25	A4-B11-C26	A4-B11-C27	A4-B11-C28	A4-B11-C29	A4-B11-C30
	A4-B11-C31	A4-B11-C32	A4-B11-C33	A4-B11-C34	A4-B11-C35	A4-B11-C36
	A4-B11-C37	A4-B11-C38	A4-B11-C39	A4-B11-C40	A4-B11-C41	A4-B11-C42
	A4-B11-C43	A4-B11-C44	A4-B11-C45	A4-B11-C46	A4-B11-C47	A4-B11-C48
	A4-B11-C49	A4-B11-C50	A4-B11-C51	A4-B11-C52	A4-B11-C53	A4-B11-C54
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	A4-B11-C61	A4-B11-C62	A4-B11-C63	A4-B11-C64	A4-B11-C65	A4-B11-C66
	A4-B11-C67	A4-B11-C68	A4-B11-C69	A4-B11-C70	A4-B11-C71	A4-B11-C72
	A4-B11-C73	A4-B11-C74	A4-B11-C75	A4-B11-C76	A4-B11-C77	A4-B11-C78
	A4-B11-C79	A4-B11-C80	A4-B11-C81	A4-B11-C82	A4-B11-C83	A4-B11-C84
25	A4-B11-C85	A4-B11-C86	A4-B11-C87	A4-B11-C88	A4-B11-C89	A4-B11-C90
	A4-B11-C91	A4-B11-C92	A4-B11-C93	A4-B11-C94	A4-B11-C95	A4-B11-C96
	A4-B11-C97	A4-B11-C98	A4-B11-C99	A4-B11-C100	A4-B11-C101	A4-B11-C102
	A4-B11-C103	A4-B11-C104	A4-B11-C105	A4-B11-C106	A4-B11-C107	A4-B11-C108
	A4-B11-C109	A4-B11-C110	A4-B11-C111	A4-B11-C112	A4-B11-C113	A4-B11-C114
30	A4-B11-C115	A4-B11-C116	A4-B11-C117	A4-B11-C118	A4-B11-C119	A4-B11-C120
	A4-B11-C121	A4-B11-C122	A4-B11-C123	A4-B11-C124	A4-B11-C125	A4-B11-C126
	A4-B11-C127	A4-B11-C128	A4-B11-C129	A4-B11-C130	A4-B11-C131	A4-B11-C132
	A4-B11-C133	A4-B11-C134	A4-B11-C135	A4-B11-C136	A4-B11-C137	A4-B11-C138
	A4-B11-C139	A4-B11-C140	BLANK	BLANK	BLANK	BLANK
35	A4-B12-C1	A4-B12-C2	A4-B12-C3	A4-B12-C4	A4-B12-C5	A4-B12-C6
	A4-B12-C7	A4-B12-C8	A4-B12-C9	A4-B12-C10	A4-B12-C11	A4-B12-C12
	A4-B12-C13	A4-B12-C14	A4-B12-C15	A4-B12-C16	A4-B12-C17	A4-B12-C18

	A4-B12-C19	A4-B12-C20	A4-B12-C21	A4-B12-C22	A4-B12-C23	A4-B12-C24
	A4-B12-C25	A4-B12-C26	A4-B12-C27	A4-B12-C28	A4-B12-C29	A4-B12-C30
	A4-B12-C31	A4-B12-C32	A4-B12-C33	A4-B12-C34	A4-B12-C35	A4-B12-C36
	A4-B12-C37	A4-B12-C38	A4-B12-C39	A4-B12-C40	A4-B12-C41	A4-B12-C42
5	A4-B12-C43	A4-B12-C44	A4-B12-C45	A4-B12-C46	A4-B12-C47	A4-B12-C48
	A4-B12-C49	A4-B12-C50	A4-B12-C51	A4-B12-C52	A4-B12-C53	A4-B12-C54
	A4-B12-C55	A4-B12-C56	A4-B12-C57	A4-B12-C58	A4-B12-C59	A4-B12-C60
	A4-B12-C61	A4-B12-C62	A4-B12-C63	A4-B12-C64	A4-B12-C65	A4-B12-C66
	A4-B12-C67	A4-B12-C68	A4-B12-C69	A4-B12-C70	A4-B12-C71	A4-B12-C72
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	A4-B12-C79	A4-B12-C80	A4-B12-C81	A4-B12-C82	A4-B12-C83	A4-B12-C84
	A4-B12-C85	A4-B12-C86	A4-B12-C87	A4-B12-C88	A4-B12-C89	A4-B12-C90
	A4-B12-C91	A4-B12-C92	A4-B12-C93	A4-B12-C94	A4-B12-C95	A4-B12-C96
	A4-B12-C97	A4-B12-C98	A4-B12-C99	A4-B12-C100	A4-B12-C101	A4-B12-C102
15	A4-B12-C103	A4-B12-C104	A4-B12-C105	A4-B12-C106	A4-B12-C107	A4-B12-C108
	A4-B12-C109	A4-B12-C110	A4-B12-C111	A4-B12-C112	A4-B12-C113	A4-B12-C114
	A4-B12-C115	A4-B12-C116	A4-B12-C117	A4-B12-C118	A4-B12-C119	A4-B12-C120
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	A4-B12-C127	A4-B12-C128	A4-B12-C129	A4-B12-C130	A4-B12-C131	A4-B12-C132
20	A4-B12-C133	A4-B12-C134	A4-B12-C135	A4-B12-C136	A4-B12-C137	A4-B12-C138
	A4-B12-C139	A4-B12-C140	BLANK	BLANK	BLANK	BLANK
	A4-B13-C1	A4-B13-C2	A4-B13-C3	A4-B13-C4	A4-B13-C5	A4-B13-C6
	A4-B13-C7	A4-B13-C8	A4-B13-C9	A4-B13-C10	A4-B13-C11	A4-B13-C12
	A4-B13-C13	A4-B13-C14	A4-B13-C15	A4-B13-C16	A4-B13-C17	A4-B13-C18
25	A4-B13-C19	A4-B13-C20	A4-B13-C21	A4-B13-C22	A4-B13-C23	A4-B13-C24
	A4-B13-C25	A4-B13-C26	A4-B13-C27	A4-B13-C28	A4-B13-C29	A4-B13-C30
	A4-B13-C31	A4-B13-C32	A4-B13-C33	A4-B13-C34	A4-B13-C35	A4-B13-C36
	A4-B13-C37	A4-B13-C38	A4-B13-C39	A4-B13-C40	A4-B13-C41	A4-B13-C42
	A4-B13-C43	A4-B13-C44	A4-B13-C45	A4-B13-C46	A4-B13-C47	A4-B13-C48
30	A4-B13-C49	A4-B13-C50	A4-B13-C51	A4-B13-C52	A4-B13-C53	A4-B13-C54
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	A4-B13-C61	A4-B13-C62	A4-B13-C63	A4-B13-C64	A4-B13-C65	A4-B13-C66
	A4-B13-C67	A4-B13-C68	A4-B13-C69	A4-B13-C70	A4-B13-C71	A4-B13-C72
	A4-B13-C73	A4-B13-C74	A4-B13-C75	A4-B13-C76	A4-B13-C77	A4-B13-C78
35	A4-B13-C79	A4-B13-C80	A4-B13-C81	A4-B13-C82	A4-B13-C83	A4-B13-C84
	A4-B13-C85	A4-B13-C86	A4-B13-C87	A4-B13-C88	A4-B13-C89	A4-B13-C90
	A4-B13-C91	A4-B13-C92	A4-B13-C93	A4-B13-C94	A4-B13-C95	A4-B13-C96

	A4-B13-C97	A4-B13-C98	A4-B13-C99	A4-B13-C100	A4-B13-C101	A4-B13-C102
	A4-B13-C103	A4-B13-C104	A4-B13-C105	A4-B13-C106	A4-B13-C107	A4-B13-C108
	A4-B13-C109	A4-B13-C110	A4-B13-C111	A4-B13-C112	A4-B13-C113	A4-B13-C114
	A4-B13-C115	A4-B13-C116	A4-B13-C117	A4-B13-C118	A4-B13-C119	A4-B13-C120
5	A4-B13-C121	A4-B13-C122	A4-B13-C123	A4-B13-C124	A4-B13-C125	A4-B13-C126
	A4-B13-C127	A4-B13-C128	A4-B13-C129	A4-B13-C130	A4-B13-C131	A4-B13-C132
	A4-B13-C133	A4-B13-C134	A4-B13-C135	A4-B13-C136	A4-B13-C137	A4-B13-C138
	A4-B13-C139	A4-B13-C140	BLANK	BLANK	BLANK	BLANK
	A5-B1-C1	A5-B1-C2	A5-B1-C3	A5-B1-C4	A5-B1-C5	A5-B1-C6
10	A5-B1-C7	A5-B1-C8	A5-B1-C9	A5-B1-C10	A5-B1-C11	A5-B1-C12
	A5-B1-C13	A5-B1-C14	A5-B1-C15	A5-B1-C16	A5-B1-C17	A5-B1-C18
	A5-B1-C19	A5-B1-C20	A5-B1-C21	A5-B1-C22	A5-B1-C23	A5-B1-C24
	A5-B1-C25	A5-B1-C26	A5-B1-C27	A5-B1-C28	A5-B1-C29	A5-B1-C30
	A5-B1-C31	A5-B1-C32	A5-B1-C33	A5-B1-C34	A5-B1-C35	A5-B1-C36
15	A5-B1-C37	A5-B1-C38	A5-B1-C39	A5-B1-C40	A5-B1-C41	A5-B1-C42
	A5-B1-C43	A5-B1-C44	A5-B1-C45	A5-B1-C46	A5-B1-C47	A5-B1-C48
	A5-B1-C49	A5-B1-C50	A5-B1-C51	A5-B1-C52	A5-B1-C53	A5-B1-C54
	A5-B1-C55	A5-B1-C56	A5-B1-C57	A5-B1-C58	A5-B1-C59	A5-B1-C60
	A5-B1-C61	A5-B1-C62	A5-B1-C63	A5-B1-C64	A5-B1-C65	A5-B1-C66
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	A5-B1-C73	A5-B1-C74	A5-B1-C75	A5-B1-C76	A5-B1-C77	A5-B1-C78
	A5-B1-C79	A5-B1-C80	A5-B1-C81	A5-B1-C82	A5-B1-C83	A5-B1-C84
	A5-B1-C85	A5-B1-C86	A5-B1-C87	A5-B1-C88	A5-B1-C89	A5-B1-C90
	A5-B1-C91	A5-B1-C92	A5-B1-C93	A5-B1-C94	A5-B1-C95	A5-B1-C96
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	A5-B1-C103	A5-B1-C104	A5-B1-C105	A5-B1-C106	A5-B1-C107	A5-B1-C108
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	A5-B1-C115	A5-B1-C116	A5-B1-C117	A5-B1-C118	A5-B1-C119	A5-B1-C120
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	A5-B1-C133	A5-B1-C134	A5-B1-C135	A5-B1-C136	A5-B1-C137	A5-B1-C138
	A5-B1-C139	A5-B1-C140	BLANK	BLANK	BLANK	BLANK
	A5-B2-C1	A5-B2-C2	A5-B2-C3	A5-B2-C4	A5-B2-C5	A5-B2-C6
	A5-B2-C7	A5-B2-C8	A5-B2-C9	A5-B2-C10	A5-B2-C11	A5-B2-C12
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	A5-B2-C19	A5-B2-C20	A5-B2-C21	A5-B2-C22	A5-B2-C23	A5-B2-C24
	A5-B2-C25	A5-B2-C26	A5-B2-C27	A5-B2-C28	A5-B2-C29	A5-B2-C30

	A5-B2-C31	A5-B2-C32	A5-B2-C33	A5-B2-C34	A5-B2-C35	A5-B2-C36
	A5-B2-C37	A5-B2-C38	A5-B2-C39	A5-B2-C40	A5-B2-C41	A5-B2-C42
	A5-B2-C43	A5-B2-C44	A5-B2-C45	A5-B2-C46	A5-B2-C47	A5-B2-C48
	A5-B2-C49	A5-B2-C50	A5-B2-C51	A5-B2-C52	A5-B2-C53	A5-B2-C54
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	A5-B2-C67	A5-B2-C68	A5-B2-C69	A5-B2-C70	A5-B2-C71	A5-B2-C72
	A5-B2-C73	A5-B2-C74	A5-B2-C75	A5-B2-C76	A5-B2-C77	A5-B2-C78
	A5-B2-C79	A5-B2-C80	A5-B2-C81	A5-B2-C82	A5-B2-C83	A5-B2-C84
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	A5-B2-C103	A5-B2-C104	A5-B2-C105	A5-B2-C106	A5-B2-C107	A5-B2-C108
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	A5-B2-C127	A5-B2-C128	A5-B2-C129	A5-B2-C130	A5-B2-C131	A5-B2-C132
	A5-B2-C133	A5-B2-C134	A5-B2-C135	A5-B2-C136	A5-B2-C137	A5-B2-C138
	A5-B2-C139	A5-B2-C140	BLANK	BLANK	BLANK	BLANK
20	A5-B3-C1	A5-B3-C2	A5-B3-C3	A5-B3-C4	A5-B3-C5	A5-B3-C6
	A5-B3-C7	A5-B3-C8	A5-B3-C9	A5-B3-C10	A5-B3-C11	A5-B3-C12
	A5-B3-C13	A5-B3-C14	A5-B3-C15	A5-B3-C16	A5-B3-C17	A5-B3-C18
	A5-B3-C19	A5-B3-C20	A5-B3-C21	A5-B3-C22	A5-B3-C23	A5-B3-C24
	A5-B3-C25	A5-B3-C26	A5-B3-C27	A5-B3-C28	A5-B3-C29	A5-B3-C30
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	A5-B3-C37	A5-B3-C38	A5-B3-C39	A5-B3-C40	A5-B3-C41	A5-B3-C42
	A5-B3-C43	A5-B3-C44	A5-B3-C45	A5-B3-C46	A5-B3-C47	A5-B3-C48
	A5-B3-C49	A5-B3-C50	A5-B3-C51	A5-B3-C52	A5-B3-C53	A5-B3-C54
	A5-B3-C55	A5-B3-C56	A5-B3-C57	A5-B3-C58	A5-B3-C59	A5-B3-C60
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	A5-B3-C73	A5-B3-C74	A5-B3-C75	A5-B3-C76	A5-B3-C77	A5-B3-C78
	A5-B3-C79	A5-B3-C80	A5-B3-C81	A5-B3-C82	A5-B3-C83	A5-B3-C84
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	A5-B3-C97	A5-B3-C98	A5-B3-C99	A5-B3-C100	A5-B3-C101	A5-B3-C102
	A5-B3-C103	A5-B3-C104	A5-B3-C105	A5-B3-C106	A5-B3-C107	A5-B3-C108

	A5-B3-C109	A5-B3-C110	A5-B3-C111	A5-B3-C112	A5-B3-C113	A5-B3-C114
	A5-B3-C115	A5-B3-C116	A5-B3-C117	A5-B3-C118	A5-B3-C119	A5-B3-C120
	A5-B3-C121	A5-B3-C122	A5-B3-C123	A5-B3-C124	A5-B3-C125	A5-B3-C126
	A5-B3-C127	A5-B3-C128	A5-B3-C129	A5-B3-C130	A5-B3-C131	A5-B3-C132
5	A5-B3-C133	A5-B3-C134	A5-B3-C135	A5-B3-C136	A5-B3-C137	A5-B3-C138
	A5-B3-C139	A5-B3-C140	BLANK	BLANK	BLANK	BLANK
	A5-B4-C1	A5-B4-C2	A5-B4-C3	A5-B4-C4	A5-B4-C5	A5-B4-C6
	A5-B4-C7	A5-B4-C8	A5-B4-C9	A5-B4-C10	A5-B4-C11	A5-B4-C12
	A5-B4-C13	A5-B4-C14	A5-B4-C15	A5-B4-C16	A5-B4-C17	A5-B4-C18
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	A5-B4-C25	A5-B4-C26	A5-B4-C27	A5-B4-C28	A5-B4-C29	A5-B4-C30
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	A5-B4-C37	A5-B4-C38	A5-B4-C39	A5-B4-C40	A5-B4-C41	A5-B4-C42
	A5-B4-C43	A5-B4-C44	A5-B4-C45	A5-B4-C46	A5-B4-C47	A5-B4-C48
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	A5-B4-C55	A5-B4-C56	A5-B4-C57	A5-B4-C58	A5-B4-C59	A5-B4-C60
	A5-B4-C61	A5-B4-C62	A5-B4-C63	A5-B4-C64	A5-B4-C65	A5-B4-C66
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	A5-B4-C91	A5-B4-C92	A5-B4-C93	A5-B4-C94	A5-B4-C95	A5-B4-C96
	A5-B4-C97	A5-B4-C98	A5-B4-C99	A5-B4-C100	A5-B4-C101	A5-B4-C102
	A5-B4-C103	A5-B4-C104	A5-B4-C105	A5-B4-C106	A5-B4-C107	A5-B4-C108
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	A5-B4-C115	A5-B4-C116	A5-B4-C117	A5-B4-C118	A5-B4-C119	A5-B4-C120
	A5-B4-C121	A5-B4-C122	A5-B4-C123	A5-B4-C124	A5-B4-C125	A5-B4-C126
	A5-B4-C127	A5-B4-C128	A5-B4-C129	A5-B4-C130	A5-B4-C131	A5-B4-C132
	A5-B4-C133	A5-B4-C134	A5-B4-C135	A5-B4-C136	A5-B4-C137	A5-B4-C138
30	A5-B4-C139	A5-B4-C140	BLANK	BLANK	BLANK	BLANK
•	A5-B5-C1	A5-B5-C2	A5-B5-C3	A5-B5-C4	A5-B5-C5	A5-B5-C6
	A5-B5-C7	A5-B5-C8	A5-B5-C9	A5-B5-C10	A5-B5-C11	A5-B5-C12
	A5-B5-C13	A5-B5-C14	A5-B5-C15	A5-B5-C16	A5-B5-C17	A5-B5-C18
	A5-B5-C19	A5-B5-C20	A5-B5-C21	A5-B5-C22	A5-B5-C23	A5-B5-C24
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	A5-B5-C37	A5-B5-C38	A5-B5-C39	A5-B5-C40	A5-B5-C41	A5-B5-C42

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	A5-B5-C43	A5-B5-C44	A5-B5-C45	A5-B5-C46	A5-B5-C47	A5-B5-C48
	A5-B5-C49	A5-B5-C50	A5-B5-C51	A5-B5-C52	A5-B5-C53	A5-B5-C54
	A5-B5-C55	A5-B5-C56	A5-B5-C57	A5-B5-C58	A5-B5-C59	A5-B5-C60
	A5-B5-C61	A5-B5-C62	A5-B5-C63	A5-B5-C64	A5-B5-C65	A5-B5-C66
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	A5-B5-C103	A5-B5-C104	A5-B5-C105	A5-B5-C106	A5-B5-C107	A5-B5-C108
	A5-B5-C109	A5-B5-C110	A5-B5-C111	A5-B5-C112	A5-B5-C113	A5-B5-C114
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	A5-B5-C133	A5-B5-C134	A5-B5-C135	A5-B5-C136	A5-B5-C137	A5-B5-C138
	A5-B5-C139	A5-B5-C140	BLANK	BLANK	BLANK	BLANK
	A5-B6-C1	A5-B6-C2	A5-B6-C3	A5-B6-C4	A5-B6-C5	A5-B6-C6
	A5-B6-C7	A5-B6-C8	A5-B6-C9	A5-B6-C10	A5-B6-C11	A5-B6-C12
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	A5-B6-C25	A5-B6-C26	A5-B6-C27	A5-B6-C28	A5-B6-C29	A5-B6-C30
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	A5-B6-C55	A5-B6-C56	A5-B6-C57	A5-B6-C58	A5-B6-C59	A5-B6-C60
	A5-B6-C61	A5-B6-C62	A5-B6-C63	A5-B6-C64	A5-B6-C65	A5-B6-C66
	A5-B6-C67	A5-B6-C68	A5-B6-C69	A5-B6-C70	A5-B6-C71	A5-B6-C72
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	A5-B6-C85	A5-B6-C86	A5-B6-C87	A5-B6-C88	A5-B6-C89	A5-B6-C90
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	A5-B6-C121	A5-B6-C122	A5-B6-C123	A5-B6-C124	A5-B6-C125	A5-B6-C126
	A5-B6-C127	A5-B6-C128	A5-B6-C129	A5-B6-C130	A5-B6-C131	A5-B6-C132
	A5-B6-C133	A5-B6-C134	A5-B6-C135	A5-B6-C136	A5-B6-C137	A5-B6-C138
	A5-B6-C139	A5-B6-C140	BLANK	BLANK	BLANK	BLANK
5	A5-B7-C1	A5-B7-C2	A5-B7-C3	A5-B7-C4	A5-B7-C5	A5-B7-C6
	A5-B7-C7	A5-B7-C8	A5-B7-C9	A5-B7-C10	A5-B7-C11	A5-B7-C12
	A5-B7-C13	A5-B7-C14	A5-B7-C15	A5-B7-C16	A5-B7-C17	A5-B7-C18
	A5-B7-C19	A5-B7-C20	A5-B7-C21	A5-B7-C22	A5-B7-C23	A5-B7-C24
	A5-B7-C25	A5-B7-C26	A5-B7-C27	A5-B7-C28	A5-B7-C29	A5-B7-C30
10	A5-B7-C31	A5-B7-C32	A5-B7-C33	A5-B7-C34	A5-B7-C35	A5-B7-C36
-	A5-B7-C37	A5-B7-C38	A5-B7-C39	A5-B7-C40	A5-B7-C41	A5-B7-C42
	A5-B7-C43	A5-B7-C44	A5-B7-C45	A5-B7-C46	A5-B7-C47	A5-B7-C48
	A5-B7-C49	A5-B7-C50	A5-B7-C51	A5-B7-C52	A5-B7-C53	A5-B7-C54
	A5-B7-C55	A5-B7-C56	A5-B7-C57	A5-B7-C58	A5-B7-C59	A5-B7-C60
15	A5-B7-C61	A5-B7-C62	A5-B7-C63	A5-B7-C64	A5-B7-C65	A5-B7-C66
	A5-B7-C67	A5-B7-C68	A5-B7-C69	A5-B7-C70	A5-B7-C71	A5-B7-C72
	A5-B7-C73	A5-B7-C74	A5-B7-C75	A5-B7-C76	A5-B7-C77	A5-B7-C78
	A5-B7-C79	A5-B7-C80	A5-B7-C81	A5-B7-C82	A5-B7-C83	A5-B7-C84
	A5-B7-C85	A5-B7-C86	A5-B7-C87	A5-B7-C88	A5-B7-C89	A5-B7-C90
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	A5-B7-C97	A5-B7-C98	A5-B7-C99	A5-B7-C100	A5-B7-C101	A5-B7-C102
	A5-B7-C103	A5-B7-C104	A5-B7-C105	A5-B7-C106	A5-B7-C107	A5-B7-C108
	A5-B7-C109	A5-B7-C110	A5-B7-C111	A5-B7-C112	A5-B7-C113	A5-B7-C114
	A5-B7-C115	A5-B7-C116	A5-B7-C117	A5-B7-C118	A5-B7-C119	A5-B7-C120
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	A5-B7-C127	A5-B7-C128	A5-B7-C129	A5-B7-C130	A5-B7-C131	A5-B7-C132
	A5-B7-C133	A5-B7-C134	A5-B7-C135	A5-B7-C136	A5-B7-C137	A5-B7-C138
	A5-B7-C139	A5-B7-C140	BLANK	BLANK	BLANK	BLANK
	A5-B8-C1	A5-B8-C2	A5-B8-C3	A5-B8-C4	A5-B8-C5	A5-B8-C6
30	A5-B8-C7	A5-B8-C8	A5-B8-C9	A5-B8-C10	A5-B8-C11	A5-B8-C12
	A5-B8-C13	A5-B8-C14	A5-B8-C15	A5-B8-C16	A5-B8-C17	A5-B8-C18
	A5-B8-C19	A5-B8-C20	A5-B8-C21	A5-B8-C22	A5-B8-C23	A5-B8-C24
	A5-B8-C25	A5-B8-C26	A5-B8-C27	A5-B8-C28	A5-B8-C29	A5-B8-C30
	A5-B8-C31	A5-B8-C32	A5-B8-C33	A5-B8-C34	A5-B8-C35	A5-B8-C36
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	A5-B8-C43	A5-B8-C44	A5-B8-C45	A5-B8-C46	A5-B8-C47	A5-B8-C48
	A5-B8-C49	A5-B8-C50	A5-B8-C51	A5-B8-C52	A5-B8-C53	A5-B8-C54

	A5-B8-C55	A5-B8-C56	A5-B8-C57	A5-B8-C58	A5-B8-C59	A5-B8-C60
	A5-B8-C61	A5-B8-C62	A5-B8-C63	A5-B8-C64	A5-B8-C65	A5-B8-C66
	A5-B8-C67	A5-B8-C68	A5-B8-C69	A5-B8-C70	A5-B8-C71	A5-B8-C72
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	A5-B8-C85	A5-B8-C86	A5-B8-C87	A5-B8-C88	A5-B8-C89	A5-B8-C90
	A5-B8-C91	A5-B8-C92	A5-B8-C93	A5-B8-C94	A5-B8-C95	A5-B8-C96
	A5-B8-C97	A5-B8-C98	A5-B8-C99	A5-B8-C100	A5-B8-C101	A5-B8-C102
	A5-B8-C103	A5-B8-C104	A5-B8-C105	A5-B8-C106	A5-B8-C107	A5-B8-C108
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	A5-B8-C121	A5-B8-C122	A5-B8-C123	A5-B8-C124	A5-B8-C125	A5-B8-C126
	A5-B8-C127	A5-B8-C128	A5-B8-C129	A5-B8-C130	A5-B8-C131	A5-B8-C132
	A5-B8-C133	A5-B8-C134	A5-B8-C135	A5-B8-C136	A5-B8-C137	A5-B8-C138
15	A5-B8-C139	A5-B8-C140	BLANK	BLANK	BLANK	BLANK
	A5-B9-C1	A5-B9-C2	A5-B9-C3	A5-B9-C4	A5-B9-C5	A5-B9-C6
	A5-B9-C7	A5-B9-C8	A5-B9-C9	A5-B9-C10	A5-B9-C11	A5-B9-C12
	A5-B9-C13	A5-B9-C14	A5-B9-C15	A5-B9-C16	A5-B9-C17	A5-B9-C18
	A5-B9-C19	A5-B9-C20	A5-B9-C21	A5-B9-C22	A5-B9-C23	A5-B9-C24
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	A5-B9-C31	A5-B9-C32	A5-B9-C33	A5-B9-C34	A5-B9-C35	A5-B9-C36
	A5-B9-C37	A5-B9-C38	A5-B9-C39	A5-B9-C40	A5-B9-C41	A5-B9-C42
	A5-B9-C43	A5-B9-C44	A5-B9-C45	A5-B9-C46	A5-B9-C47	A5-B9-C48
	A5-B9-C49	A5-B9-C50	A5-B9-C51	A5-B9-C52	A5-B9-C53	A5-B9-C54
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	A5-B9-C97	A5-B9-C98	A5-B9-C99	A5-B9-C100	A5-B9-C101	A5-B9-C102
	A5-B9-C103	A5-B9-C104	A5-B9-C105	A5-B9-C106	A5-B9-C107	A5-B9-C108
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	A5-B9-C121	A5-B9-C122	A5-B9-C123	A5-B9-C124	A5-B9-C125	A5-B9-C126
	A5-B9-C127	A5-B9-C128	A5-B9-C129	A5-B9-C130	A5-B9-C131	A5-B9-C132

	A5-B9-C133	A5-B9-C134	A5-B9-C135	A5-B9-C136	A5-B9-C137	A5-B9-C138
	A5-B9-C139	A5-B9-C140	BLANK	BLANK	BLANK	BLANK
	A5-B10-C1	A5-B10-C2	A5-B10-C3	A5-B10-C4	A5-B10-C5	A5-B10-C6
	A5-B10-C7	A5-B10-C8	A5-B10-C9	A5-B10-C10	A5-B10-C11	A5-B10-C12
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	A5-B10-C19	A5-B10-C20	A5-B10-C21	A5-B10-C22	A5-B10-C23	A5-B10-C24
	A5-B10-C25	A5-B10-C26	A5-B10-C27	A5-B10-C28	A5-B10-C29	A5-B10-C30
	A5-B10-C31	A5-B10-C32	A5-B10-C33	A5-B10-C34	A5-B10-C35	A5-B10-C36
	A5-B10-C37	A5-B10-C38	A5-B10-C39	A5-B10-C40	A5-B10-C41	A5-B10-C42
10	A5-B10-C43	A5-B10-C44	A5-B10-C45	A5-B10-C46	A5-B10-C47	A5-B10-C48
	A5-B10-C49	A5-B10-C50	A5-B10-C51	A5-B10-C52	A5-B10-C53	A5-B10-C54
	A5-B10-C55	A5-B10-C56	A5-B10-C57	A5-B10-C58	A5-B10-C59	A5-B10-C60
	A5-B10-C61	A5-B10-C62	A5-B10-C63	A5-B10-C64	A5-B10-C65	A5-B10-C66
	A5-B10-C67	A5-B10-C68	A5-B10-C69	A5-B10-C70	A5-B10-C71	A5-B10-C72
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	A5-B10-C79	A5-B10-C80	A5-B10-C81	A5-B10-C82	A5-B10-C83	A5-B10-C84
	A5-B10-C85	A5-B10-C86	A5-B10-C87	A5-B10-C88	A5-B10-C89	A5-B10-C90
	A5-B10-C91	A5-B10-C92	A5-B10-C93	A5-B10-C94	A5-B10-C95	A5-B10-C96
	A5-B10-C97	A5-B10-C98	A5-B10-C99	A5-B10-C100	A5-B10-C101	A5-B10-C102
20	A5-B10-C103	A5-B10-C104	A5-B10-C105	A5-B10-C106	A5-B10-C107	A5-B10-C108
	A5-B10-C109	A5-B10-C110	A5-B10-C111	A5-B10-C112	A5-B10-C113	A5-B10-C114
	A5-B10-C115	A5-B10-C116	A5-B10-C117	A5-B10-C118	A5-B10-C119	A5-B10-C120
	A5-B10-C121	A5-B10-C122	A5-B10-C123	A5-B10-C124	A5-B10-C125	A5-B10-C126
	A5-B10-C127	A5-B10-C128	A5-B10-C129	A5-B10-C130	A5-B10-C131	A5-B10-C132
25	A5-B10-C133	A5-B10-C134	A5-B10-C135	A5-B10-C136	A5-B10-C137	A5-B10-C138
	A5-B10-C139	A5-B10-C140	BLANK	BLANK	BLANK	BLANK
	A5-B11-C1	A5-B11-C2	A5-B11-C3	A5-B11-C4	A5-B11-C5	A5-B11-C6
	A5-B11-C7	A5-B11-C8	A5-B11-C9	A5-B11-C10	A5-B11-C11	A5-B11-C12
	A5-B11-C13	A5-B11-C14	A5-B11-C15	A5-B11-C16	A5-B11-C17	A5-B11-C18
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	A5-B11-C25	A5-B11-C26	A5-B11-C27	A5-B11-C28	A5-B11-C29	A5-B11-C30
	A5-B11-C31	A5-B11-C32	A5-B11-C33	A5-B11-C34	A5-B11-C35	A5-B11-C36
	A5-B11-C37	A5-B11-C38	A5-B11-C39	A5-B11-C40	A5-B11-C41	A5-B11-C42
	A5-B11-C43	A5-B11-C44	A5-B11-C45	A5-B11-C46	A5-B11-C47	A5-B11-C48
35	A5-B11-C49	A5-B11-C50	A5-B11-C51	A5-B11-C52	A5-B11-C53	A5-B11-C54
	A5-B11-C55	A5-B11-C56	A5-B11-C57	A5-B11-C58	A5-B11-C59	A5-B11-C60
	A5-B11-C61	A5-B11-C62	A5-B11-C63	A5-B11-C64	A5-B11-C65	A5-B11-C66

	A5-B11-C67	A5-B11-C68	A5-B11-C69	A5-B11-C70	A5-B11-C71	A5-B11-C72
	A5-B11-C73	A5-B11-C74	A5-B11-C75	A5-B11-C76	A5-B11-C77	A5-B11-C78
	A5-B11-C79	A5-B11-C80	A5-B11-C81	A5-B11-C82	A5-B11-C83	A5-B11-C84
	A5-B11-C85	A5-B11-C86	A5-B11-C87	A5-B11-C88	A5-B11-C89	A5-B11-C90
5	A5-B11-C91	A5-B11-C92	A5-B11-C93	A5-B11-C94	A5-B11-C95	A5-B11-C96
	A5-B11-C97	A5-B11-C98	A5-B11-C99	A5-B11-C100	A5-B11-C101	A5-B11-C102
	A5-B11-C103	A5-B11-C104	A5-B11-C105	A5-B11-C106	A5-B11-C107	A5-B11-C108
	A5-B11-C109	A5-B11-C110	A5-B11-C111	A5-B11-C112	A5-B11-C113	A5-B11-C114
	A5-B11-C115	A5-B11-C116	A5-B11-C117	A5-B11-C118	A5-B11-C119	A5-B11-C120
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	A5-B11-C127	A5-B11-C128	A5-B11-C129	A5-B11-C130	A5-B11-C131	A5-B11-C132
	A5-B11-C133	A5-B11-C134	A5-B11-C135	A5-B11-C136	A5-B11-C137	A5-B11-C138
	A5-B11-C139	A5-B11-C140	BLANK	BLANK	BLANK	BLANK
	A5-B12-C1	A5-B12-C2	A5-B12-C3	A5-B12-C4	A5-B12-C5	A5-B12-C6
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	A5-B12-C13	A5-B12-C14	A5-B12-C15	A5-B12-C16	A5-B12-C17	A5-B12-C18
	A5-B12-C19	A5-B12-C20	A5-B12-C21	A5-B12-C22	A5-B12-C23	A5-B12-C24
	A5-B12-C25	A5-B12-C26	A5-B12-C27	A5-B12-C28	A5-B12-C29	A5-B12-C30
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	A5-B12-C43	A5-B12-C44	A5-B12-C45	A5-B12-C46	A5-B12-C47	A5-B12-C48
	A5-B12-C49	A5-B12-C50	A5-B12-C51	A5-B12-C52	A5-B12-C53	A5-B12-C54
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	A5-B12-C103	A5-B12-C104	A5-B12-C105	A5-B12-C106	A5-B12-C107	A5-B12-C108
	A5-B12-C109	A5-B12-C110	A5-B12-C111	A5-B12-C112	A5-B12-C113	A5-B12-C114
	A5-B12-C115	A5-B12-C116	A5-B12-C117	A5-B12-C118	A5-B12-C119	A5-B12-C120
	A5-B12-C121	A5-B12-C122	A5-B12-C123	A5-B12-C124	A5-B12-C125	A5-B12-C126
35	A5-B12-C127	A5-B12-C128	A5-B12-C129	A5-B12-C130	A5-B12-C131	A5-B12-C132
	A5-B12-C133	A5-B12-C134	A5-B12-C135	A5-B12-C136	A5-B12-C137	A5-B12-C138
	A5-B12-C139	A5-B12-C140	BLANK	BLANK	BLANK	BLANK

	A5-B13-C1	A5-B13-C2	A5-B13-C3	A5-B13-C4	A5-B13-C5	A5-B13-C6
	A5-B13-C7	A5-B13-C8	A5-B13-C9	A5-B13-C10	A5-B13-C11	A5-B13-C12
	A5-B13-C13	A5-B13-C14	A5-B13-C15	A5-B13-C16	A5-B13-C17	A5-B13-C18
	A5-B13-C19	A5-B13-C20	A5-B13-C21	A5-B13-C22	A5-B13-C23	A5-B13-C24
5	A5-B13-C25	A5-B13-C26	A5-B13-C27	A5-B13-C28	A5-B13-C29	A5-B13-C30
	A5-B13-C31	A5-B13-C32	A5-B13-C33	A5-B13-C34	A5-B13-C35	A5-B13-C36
	A5-B13-C37	A5-B13-C38	A5-B13-C39	A5-B13-C40	A5-B13-C41	A5-B13-C42
	A5-B13-C43	A5-B13-Ç44	A5-B13-C45	A5-B13-C46	A5-B13-C47	A5-B13-C48
	A5-B13-C49	A5-B13-C50	A5-B13-C51	A5-B13-C52	A5-B13-C53	A5-B13-C54
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	A5-B13-C61	A5-B13-C62	A5-B13-C63	A5-B13-C64	A5-B13-C65	A5-B13-C66
	A5-B13-C67	A5-B13-C68	A5-B13-C69	A5-B13-C70	A5-B13-C71	A5-B13-C72
	A5-B13-C73	A5-B13-C74	A5-B13-C75	A5-B13-C76	A5-B13-C77	A5-B13-C78
	A5-B13-C79	A5-B13-C80	A5-B13-C81	A5-B13-C82	A5-B13-C83	A5-B13-C84
15	A5-B13-C85	A5-B13-C86	A5-B13-C87	A5-B13-C88	A5-B13-C89	. A5-B13-C90
	A5-B13-C91	A5-B13-C92	A5-B13-C93	A5-B13-C94	A5-B13-C95	A5-B13-C96
	A5-B13-C97	A5-B13-C98	A5-B13-C99	A5-B13-C100	A5-B13-C101	A5-B13-C102
	A5-B13-C103	A5-B13-C104	A5-B13-C105	A5-B13-C106	A5-B13-C107	A5-B13-C108
	A5-B13-C109	A5-B13-C110	A5-B13-C111	A5-B13-C112	A5-B13-C113	A5-B13-C114
20	A5-B13-C115	A5-B13-C116	A5-B13-C117	A5-B13-C118	A5-B13-C119	A5-B13-C120
	A5-B13-C121	A5-B13-C122	A5-B13-C123	A5-B13-C124	A5-B13-C125	A5-B13-C126
	A5-B13-C127	A5-B13-C128	A5-B13-C129	A5-B13-C130	A5-B13-C131	A5-B13-C132
	A5-B13-C133	A5-B13-C134	A5-B13-C135	A5-B13-C136	A5-B13-C137	A5-B13-C138
	A5-B13-C139	A5-B13-C140	BLANK	BLANK	BLANK	BLANK
25	A6-B1-C1	A6-B1-C2	A6-B1-C3	A6-B1-C4	A6-B1-C5	A6-B1-C6
	A6-B1-C7	A6-B1-C8	A6-B1-C9	A6-B1-C10	A6-B1-C11	A6-B1-C12
	A6-B1-C13	A6-B1-C14	A6-B1-C15	A6-B1-C16	A6-B1-C17	A6-B1-C18
	A6-B1-C19	A6-B1-C20	A6-B1-C21	A6-B1-C22	A6-B1-C23	A6-B1-C24
	A6-B1-C25	A6-B1-C26	A6-B1-C27	A6-B1-C28	A6-B1-C29	A6-B1-C30
30	A6-B1-C31	A6-B1-C32	A6-B1-C33	A6-B1-C34	A6-B1-C35	A6-B1-C36
	A6-B1-C37	A6-B1-C38	A6-B1-C39	A6-B1-C40	A6-B1-C41	A6-B1-C42
	A6-B1-C43	A6-B1-C44	A6-B1-C45	A6-B1-C46	A6-B1-C47	A6-B1-C48
	A6-B1-C49	A6-B1-C50	A6-B1-C51	A6-B1-C52	A6-B1-C53	A6-B1-C54
	A6-B1-C55	A6-B1-C56	A6-B1-C57	A6-B1-C58	A6-B1-C59	A6-B1-C60
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	A6-B1-C67	A6-B1-C68	A6-B1-C69	A6-B1-C70	A6-B1-C71	A6-B1-C72
	A6-B1-C73	A6-B1-C74	A6-B1-C75	A6-B1-C76	A6-B1-C77	A6-B1-C78

	A6-B1-C79	A6-B1-C80	A6-B1-C81	A6-B1-C82	A6-B1-C83	A6-B1-C84
	A6-B1-C85	A6-B1-C86	A6-B1-C87	A6-B1-C88	A6-B1-C89	A6-B1-C90
	A6-B1-C91	A6-B1-C92	A6-B1-C93	A6-B1-C94	A6-B1-C95	A6-B1-C96
	A6-B1-C97	A6-B1-C98	A6-B1-C99	A6-B1-C100	A6-B1-C101	A6-B1-C102
5	A6-B1-C103	A6-B1-C104	A6-B1-C105	A6-B1-C106	A6-B1-C107	A6-B1-C108
	A6-B1-C109	A6-B1-C110	A6-B1-C111	A6-B1-C112	A6-B1-C113	A6-B1-C114
	A6-B1-C115	A6-B1-C116	A6-B1-C117	A6-B1-C118	A6-B1-C119	A6-B1-C120
	A6-B1-C121	A6-B1-C122	A6-B1-C123	A6-B1-C124	A6-B1-C125	A6-B1-C126
	A6-B1-C127	A6-B1-C128	A6-B1-C129	A6-B1-C130	A6-B1-C131	A6-B1-C132
10	A6-B1-C133	A6-B1-C134	A6-B1-C135	A6-B1-C136	A6-B1-C137	A6-B1-C138
	A6-B1-C139	A6-B1-C140	BLANK	BLANK	BLANK	BLANK
	A6-B2-C1	A6-B2-C2	A6-B2-C3	A6-B2-C4	A6-B2-C5	A6-B2-C6
	A6-B2-C7	A6-B2-C8	A6-B2-C9	A6-B2-C10	A6-B2-C11	A6-B2-C12
	A6-B2-C13	A6-B2-C14	A6-B2-C15	A6-B2-C16	A6-B2-C17	A6-B2-C18
15	A6-B2-C19	A6-B2-C20	A6-B2-C21	A6-B2-C22	A6-B2-C23	A6-B2-C24
	A6-B2-C25	A6-B2-C26	A6-B2-C27	A6-B2-C28	A6-B2-C29	A6-B2-C30
	A6-B2-C31	A6-B2-C32	A6-B2-C33	A6-B2-C34	A6-B2-C35	A6-B2-C36
	A6-B2-C37	A6-B2-C38	A6-B2-C39	A6-B2-C40	A6-B2-C41	A6-B2-C42
	A6-B2-C43	A6-B2-C44	A6-B2-C45	A6-B2-C46	A6-B2-C47	A6-B2-C48
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	A6-B2-C55	A6-B2-C56	A6-B2-C57	A6-B2-C58	A6-B2-C59	A6-B2-C60
	A6-B2-C61	A6-B2-C62	A6-B2-C63	A6-B2-C64	A6-B2-C65	A6-B2-C66
	A6-B2-C67	A6-B2-C68	A6-B2-C69	A6-B2-C70	A6-B2-C71	A6-B2-C72
	A6-B2-C73	A6-B2-C74	A6-B2-C75	A6-B2-C76	A6-B2-C77	A6-B2-C78
25	A6-B2-C79	A6-B2-C80	A6-B2-C81	A6-B2-C82	A6-B2-C83	A6-B2-C84
	A6-B2-C85	A6-B2-C86	A6-B2-C87	A6-B2-C88	A6-B2-C89	A6-B2-C90
	A6-B2-C91	A6-B2-C92	A6-B2-C93	A6-B2-C94	A6-B2-C95	A6-B2-C96
	A6-B2-C97	A6-B2-C98	A6-B2-C99	A6-B2-C100	A6-B2-C101	A6-B2-C102
	A6-B2-C103	A6-B2-C104	A6-B2-C105	A6-B2-C106	A6-B2-C107	A6-B2-C108
30	A6-B2-C109	A6-B2-C110	A6-B2-C111	A6-B2-C112	A6-B2-C113	A6-B2-C114
	A6-B2-C115	A6-B2-C116	A6-B2-C117	A6-B2-C118	A6-B2-C119	A6-B2-C120
	A6-B2-C121	A6-B2-C122	A6-B2-C123	A6-B2-C124	A6-B2-C125	A6-B2-C126
	A6-B2-C127	A6-B2-C128	A6-B2-C129	A6-B2-C130	A6-B2-C131	A6-B2-C132
	A6-B2-C133	A6-B2-C134	A6-B2-C135	A6-B2-C136	A6-B2-C137	A6-B2-C138
35	A6-B2-C139	A6-B2-C140	BLANK .	BLANK	BLANK	BLANK
	A6-B3-C1	A6-B3-C2	A6-B3-C3	A6-B3-C4	A6-B3-C5	A6-B3-C6
	A6-B3-C7	A6-B3-C8	A6-B3-C9	A6-B3-C10	A6-B3-C11	A6-B3-C12

	A6-B3-C13	A6-B3-C14	A6-B3-C15	A6-B3-C16	A6-B3-C17	A6-B3-C18
	A6-B3-C19	A6-B3-C20	A6-B3-C21	A6-B3-C22	A6-B3-C23	A6-B3-C24
	A6-B3-C25	A6-B3-C26	A6-B3-C27	A6-B3-C28	A6-B3-C29	A6-B3-C30
	A6-B3-C31	A6-B3-C32	A6-B3-C33	A6-B3-C34	A6-B3-C35	A6-B3-C36
5	A6-B3-C37	A6-B3-C38	A6-B3-C39	A6-B3-C40	A6-B3-C41	A6-B3-C42
	A6-B3-C43	A6-B3-C44	A6-B3-C45	A6-B3-C46	A6-B3-C47	A6-B3-C48
	A6-B3-C49	A6-B3-C50	A6-B3-C51	A6-B3-C52	A6-B3-C53	A6-B3-C54
	A6-B3-C55	A6-B3-C56	A6-B3-C57	A6-B3-C58	A6-B3-C59	A6-B3-C60
	A6-B3-C61	A6-B3-C62	A6-B3-C63	A6-B3-C64	A6-B3-C65	A6-B3-C66
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	A6-B3-C73	A6-B3-C74	A6-B3-C75	A6-B3-C76	A6-B3-C77	A6-B3-C78
	A6-B3-C79	A6-B3-C80	A6-B3-C81	A6-B3-C82	A6-B3-C83	A6-B3-C84
	A6-B3-C85	A6-B3-C86	A6-B3-C87	A6-B3-C88	A6-B3-C89	A6-B3-C90
	A6-B3-C91	A6-B3-C92	A6-B3-C93	A6-B3-C94	A6-B3-C95	A6-B3-C96
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	A6-B3-C103	A6-B3-C104	A6-B3-C105	A6-B3-C106	A6-B3-C107	A6-B3-C108
	A6-B3-C109	A6-B3-C110	A6-B3-C111	A6-B3-C112	A6-B3-C113	A6-B3-C114
	A6-B3-C115	A6-B3-C116	A6-B3-C117	A6-B3-C118	A6-B3-C119	A6-B3-C120
	A6-B3-C121	A6-B3-C122	A6-B3-C123	A6-B3-C124	A6-B3-C125	A6-B3-C126
20	A6-B3-C127	A6-B3-C128	A6-B3-C129	A6-B3-C130	A6-B3-C131	A6-B3-C132
	A6-B3-C133	A6-B3-C134	A6-B3-C135	A6-B3-C136	A6-B3-C137	A6-B3-C138
	A6-B3-C139	A6-B3-C140	BLANK	BLANK	BLANK	BLANK
	A6-B4-C1	A6-B4-C2	A6-B4-C3	A6-B4-C4	A6-B4-C5	A6-B4-C6
	A6-B4-C7	A6-B4-C8	A6-B4-C9	A6-B4-C10	A6-B4-C11	A6-B4-C12
25	A6-B4-C13	A6-B4-C14	A6-B4-C15	A6-B4-C16	A6-B4-C17	A6-B4-C18
	A6-B4-C19	A6-B4-C20	A6-B4-C21	A6-B4-C22	A6-B4-C23	A6-B4-C24
	A6-B4-C25	A6-B4-C26	A6-B4-C27	A6-B4-C28	A6-B4-C29	A6-B4-C30
	A6-B4-C31	A6-B4-C32	A6-B4-C33	A6-B4-C34	A6-B4-C35	A6-B4-C36
	A6-B4-C37	A6-B4-C38	A6-B4-C39	A6-B4-C40	A6-B4-C41	A6-B4-C42.
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	A6-B4-C49	A6-B4-C50	A6-B4-C51	A6-B4-C52	A6-B4-C53	A6-B4-C54
	A6-B4-C55	A6-B4-C56	A6-B4-C57	A6-B4-C58	A6-B4-C59	A6-B4-C60
	A6-B4-C61	A6-B4-C62	A6-B4-C63	A6-B4-C64	A6-B4-C65	A6-B4-C66
	A6-B4-C67	A6-B4-C68	A6-B4-C69	A6-B4-C70	A6-B4-C71	A6-B4-C72
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	A6-B4-C79	A6-B4-C80	A6-B4-C81	A6-B4-C82	A6-B4-C83	A6-B4-C84
	A6-B4-C85	A6-B4-C86	A6-B4-C87	A6-B4-C88	A6-B4-C89	A6-B4-C90

	A6-B4-C91	A6-B4-C92	A6-B4-C93	A6-B4-C94	A6-B4-C95	A6-B4-C96
	A6-B4-C97	A6-B4-C98	A6-B4-C99	A6-B4-C100	A6-B4-C101	A6-B4-C102
	A6-B4-C103	A6-B4-C104	A6-B4-C105	A6-B4-C106	A6-B4-C107	A6-B4-C108
	A6-B4-C109	A6-B4-C110	A6-B4-C111	A6-B4-C112	A6-B4-C113	A6-B4-C114
5	A6-B4-C115	A6-B4-C116	A6-B4-C117	A6-B4-C118	A6-B4-C119	A6-B4-C120
	A6-B4-C121	A6-B4-C122	A6-B4-C123	A6-B4-C124	A6-B4-C125	A6-B4-C126
	A6-B4-C127	A6-B4-C128	A6-B4-C129	A6-B4-C130	A6-B4-C131	A6-B4-C132
	A6-B4-C133	A6-B4-C134	A6-B4-C135	A6-B4-C136	A6-B4-C137	A6-B4-C138
	A6-B4-C139	A6-B4-C140	BLANK	BLANK	BLANK	BLANK
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	A6-B5-C7	A6-B5-C8	A6-B5-C9	A6-B5-C10	A6-B5-C11	A6-B5-C12
	A6-B5-C13	A6-B5-C14	A6-B5-C15	A6-B5-C16	A6-B5-C17	A6-B5-C18
	A6-B5-C19	A6-B5-C20	A6-B5-C21	A6-B5-C22	A6-B5-C23	A6-B5-C24
	A6-B5-C25	A6-B5-C26	A6-B5-C27	A6-B5-C28	A6-B5-C29	A6-B5-C30
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	A6-B5-C43	A6-B5-C44	A6-B5-C45	A6-B5-C46	A6-B5-C47	A6-B5-C48
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	A6-B5-C67	A6-B5-C68	A6-B5-C69	A6-B5-C70	A6-B5-C71	A6-B5-C72
	A6-B5-C73	A6-B5-C74	A6-B5-C75	A6-B5-C76	A6-B5-C77	A6-B5-C78
	A6-B5-C79	A6-B5-C80	A6-B5-C81	A6-B5-C82	A6-B5-C83	A6-B5-C84
	A6-B5-C85	A6-B5-C86	A6-B5-C87	A6-B5-C88	A6-B5-C89	A6-B5-C90
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	A6-B5-C97	A6-B5-C98	A6-B5-C99	A6-B5-C100	A6-B5-C101	A6-B5-C102
	A6-B5-C103	A6-B5-C104	A6-B5-C105	A6-B5-C106	A6-B5-C107	A6-B5-C108
	A6-B5-C109	A6-B5-C110	A6-B5-C111	A6-B5-C112	A6-B5-C113	A6-B5-C114
	A6-B5-C115	A6-B5-C116	A6-B5-C117	A6-B5-C118	A6-B5-C119	A6-B5-C120
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	A6-B5-C127	A6-B5-C128	A6-B5-C129	A6-B5-C130	A6-B5-C131	A6-B5-C132
	A6-B5-C133	A6-B5-C134	A6-B5-C135	A6-B5-C136	A6-B5-C137	A6-B5-C138
	A6-B5-C139	A6-B5-C140	BLANK	BLANK	BLANK	BLANK
	A6-B6-C1	A6-B6-C2	A6-B6-C3	A6-B6-C4	A6-B6-C5	A6-B6-C6
35	A6-B6-C7	A6-B6-C8	A6-B6-C9	A6-B6-C10	A6-B6-C11	A6-B6-C12
	A6-B6-C13	A6-B6-C14	A6-B6-C15	A6-B6-C16	A6-B6-C17	A6-B6-C18
	A6-B6-C19	A6-B6-C20	A6-B6-C21	A6-B6-C22	A6-B6-C23	A6-B6-C24

	A6-B6-C25	A6-B6-C26	A6-B6-C27	A6-B6-C28	A6-B6-C29	A6-B6-C30
	A6-B6-C31	A6-B6-C32	A6-B6-C33	A6-B6-C34	A6-B6-C35	A6-B6-C36
	A6-B6-C37	A6-B6-C38	A6-B6-C39	A6-B6-C40	A6-B6-C41	A6-B6-C42
	A6-B6-C43	A6-B6-C44	A6-B6-C45	A6-B6-C46	A6-B6-C47	A6-B6-C48
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	A6-B6-C55	A6-B6-C56	A6-B6-C57	A6-B6-C58	A6-B6-C59	A6-B6-C60
	A6-B6-C61	A6-B6-C62	A6-B6-C63	A6-B6-C64	A6-B6-C65	A6-B6-C66
	A6-B6-C67	A6-B6-C68	A6-B6-C69	A6-B6-C70	A6-B6-C71	A6-B6-C72
	A6-B6-C73	A6-B6-C74	A6-B6-C75	A6-B6-C76	A6-B6-C77	A6-B6-C78
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	A6-B6-C85	A6-B6-C86	A6-B6-C87	A6-B6-C88	A6-B6-C89	A6-B6-C90
	A6-B6-C91	A6-B6-C92	A6-B6-C93	A6-B6-C94	A6-B6-C95	A6-B6-C96
	A6-B6-C97	A6-B6-C98	A6-B6-C99	A6-B6-C100	A6-B6-C101	A6-B6-C102
	A6-B6-C103	A6-B6-C104	A6-B6-C105	A6-B6-C106	A6-B6-C107	A6-B6-C108
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	A6-B6-C115	A6-B6-C116	A6-B6-C117	A6-B6-C118	A6-B6-C119	A6-B6-C120
	A6-B6-C121	A6-B6-C122	.A6-B6-C123	A6-B6-C124	A6-B6-C125	A6-B6-C126
	A6-B6-C127	A6-B6-C128	A6-B6-C129	A6-B6-C130	A6-B6-C131	A6-B6-C132
	A6-B6-C133	A6-B6-C134	A6-B6-C135	A6-B6-C136	A6-B6-C137	A6-B6-C138
20	A6-B6-C139	A6-B6-C140	BLANK	BLANK	BLANK	BLANK
	A6-B7-C1	A6-B7-C2	A6-B7-C3	A6-B7-C4	A6-B7-C5	A6-B7-C6
	A6-B7-C7	A6-B7-C8	A6-B7-C9	A6-B7-C10	A6-B7-C11	A6-B7-C12
	A6-B7-C13	A6-B7-C14	A6-B7-C15	A6-B7-C16	A6-B7-C17	A6-B7-C18
	A6-B7-C19	A6-B7-C20	A6-B7-C21	A6-B7-C22	A6-B7-C23	A6-B7-C24
25	A6-B7-C25	A6-B7-C26	A6-B7-C27	A6-B7-C28	A6-B7-C29	A6-B7-C30
	A6-B7-C31	A6-B7-C32	A6-B7-C33	A6-B7-C34	A6-B7-C35	A6-B7-C36
	A6-B7-C37	A6-B7-C38	A6-B7-C39	A6-B7-C40	A6-B7-C41	A6-B7-C42
	A6-B7-C43	A6-B7-C44	A6-B7-C45	A6-B7-C46	A6-B7-C47	A6-B7-C48
	A6-B7-C49	A6-B7-C50	A6-B7-C51	A6-B7-C52	A6-B7-C53	A6-B7-C54
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	A6-B7-C61	A6-B7-C62	A6-B7-C63	A6-B7-C64	A6-B7-C65	A6-B7-C66
	A6-B7-C67	A6-B7-C68	A6-B7-C69	A6-B7-C70	A6-B7-C71	A6-B7-C72
	A6-B7-C73	A6-B7-C74	A6-B7-C75	A6-B7-C76	A6-B7-C77	A6-B7-C78
	A6-B7-C79	A6-B7-C80	A6-B7-C81	A6-B7-C82	A6-B7-C83	A6-B7-C84
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	A6-B7-C91	A6-B7-C92	A6-B7-C93	A6-B7-C94	A6-B7-C95	A6-B7-C96
	A6-B7-C97	A6-B7-C98	A6-B7-C99	A6-B7-C100	A6-B7-C101	A6-B7-C102

	A6-B7-C103	A6-B7-C104	A6-B7-C105	A6-B7-C106	A6-B7-C107	A6-B7-C108
	A6-B7-C109	A6-B7-C110	A6-B7-C111	A6-B7-C112	A6-B7-C113	A6-B7-C114
	A6-B7-C115	A6-B7-C116	A6-B7-C117	A6-B7-C118	A6-B7-C119	A6-B7-C120
	A6-B7-C121	A6-B7-C122	A6-B7-C123	A6-B7-C124	A6-B7-C125	A6-B7-C126
5	A6-B7-C127	A6-B7-C128	A6-B7-C129	A6-B7-C130	A6-B7-C131	A6-B7-C132
	A6-B7-C133	A6-B7-C134	A6-B7-C135	A6-B7-C136	A6-B7-C137	A6-B7-C138
	A6-B7-C139	A6-B7-C140	BLANK	BLANK	BLANK	BLANK
	A6-B8-C1	A6-B8-C2	A6-B8-C3	A6-B8-C4	A6-B8-C5	A6-B8-C6
	A6-B8-C7	A6-B8-C8	A6-B8-C9	A6-B8-C10	A6-B8-C11	A6-B8-C12
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	A6-B8-C19	A6-B8-C20	A6-B8-C21	A6-B8-C22	A6-B8-C23	A6-B8-C24
	A6-B8-C25	A6-B8-C26	A6-B8-C27	A6-B8-C28	A6-B8-C29	A6-B8-C30
	A6-B8-C31	A6-B8-C32	A6-B8-C33	A6-B8-C34	A6-B8-C35	A6-B8-C36
	A6-B8-C37	A6-B8-C38	A6-B8-C39	A6-B8-C40	A6-B8-C41	A6-B8-C42
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	A6-B8-C49	A6-B8-C50	A6-B8-C51	A6-B8-C52	A6-B8-C53	A6-B8-C54
	A6-B8-C55	A6-B8-C56	A6-B8-C57	A6-B8-C58	A6-B8-C59	A6-B8-C60
	A6-B8-C61	A6-B8-C62	A6-B8-C63	A6-B8-C64	A6-B8-C65	A6-B8-C66
	A6-B8-C67	A6-B8-C68	A6-B8-C69	A6-B8-C70	A6-B8-C71	A6-B8-C72
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	A6-B8-C79	A6-B8-C80	A6-B8-C81	A6-B8-C82	A6-B8-C83	A6-B8-C84
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	A6-B8-C91	A6-B8-C92	A6-B8-C93	A6-B8-C94	A6-B8-C95	A6-B8-C96
	A6-B8-C97	A6-B8-C98	A6-B8-C99	A6-B8-C100	A6-B8-C101	A6-B8-C102
25	A6-B8-C103	A6-B8-C104	A6-B8-C105	A6-B8-C106	A6-B8-C107	A6-B8-C108
-	A6-B8-C109	A6-B8-C110	A6-B8-C111	A6-B8-C112	A6-B8-C113	A6-B8-C114
	A6-B8-C115	A6-B8-C116	A6-B8-C117	A6-B8-C118	A6-B8-C119	A6-B8-C120
	A6-B8-C121	A6-B8-C122	A6-B8-C123	A6-B8-C124	A6-B8-C125	A6-B8-C126
	A6-B8-C127	A6-B8-C128	A6-B8-C129	A6-B8-C130	A6-B8-C131	A6-B8-C132
30	A6-B8-C133	A6-B8-C134	A6-B8-C135	A6-B8-C136	A6-B8-C137	A6-B8-C138
	A6-B8-C139	A6-B8-C140	BLANK	BLANK	BLANK	BLANK
	A6-B9-C1	A6-B9-C2	A6-B9-C3	A6-B9-C4	A6-B9-C5	A6-B9-C6
	A6-B9-C7	A6-B9-C8	A6-B9-C9	A6-B9-C10	A6-B9-C11	A6-B9-C12
	A6-B9-C13	A6-B9-C14	A6-B9-C15	A6-B9-C16	A6-B9-C17	A6-B9-C18
35	A6-B9-C19	A6-B9-C20	A6-B9-C21	A6-B9-C22	A6-B9-C23	A6-B9-C24
	A6-B9-C25	A6-B9-C26	A6-B9-C27	A6-B9-C28	A6-B9-C29	A6-B9-C30
	A6-B9-C31	A6-B9-C32	A6-B9-C33	A6-B9-C34	A6-B9-C35	A6-B9-C36

	A6-B9-C37	A6-B9-C38	A6-B9-C39	A6-B9-C40	A6-B9-C41	A6-B9-C42
	A6-B9-C43	A6-B9-C44	A6-B9-C45	A6-B9-C46	A6-B9-C47	A6-B9-C48
	A6-B9-C49	A6-B9-C50	A6-B9-C51	A6-B9-C52	A6-B9-C53	A6-B9-C54
	A6-B9-C55	A6-B9-C56	A6-B9-C57	A6-B9-C58	A6-B9-C59	A6-B9-C60
5	A6-B9-C61	A6-B9-C62	A6-B9-C63	A6-B9-C64	A6-B9-C65	A6-B9-C66
	A6-B9-C67	A6-B9-C68	A6-B9-C69	A6-B9-C70	A6-B9-C71	A6-B9-C72
	A6-B9-C73	A6-B9-C74	A6-B9-C75	A6-B9-C76	A6-B9-C77	A6-B9-C78
	A6-B9-C79	A6-B9-C80	A6-B9-C81	A6-B9-C82	A6-B9-C83	A6-B9-C84
	A6-B9-C85	A6-B9-C86	A6-B9-C87	A6-B9-C88	A6-B9-C89	A6-B9-C90
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	A6-B9-C97	A6-B9-C98	A6-B9-C99	A6-B9-C100	A6-B9-C101	A6-B9-C102
	A6-B9-C103	A6-B9-C104	A6-B9-C105	A6-B9-C106	A6-B9-C107	A6-B9-C108
	A6-B9-C109	A6-B9-C110	A6-B9-C111	A6-B9-C112	A6-B9-C113	A6-B9-C114
	A6-B9-C115	A6-B9-C116	A6-B9-C117	A6-B9-C118	A6-B9-C119	A6-B9-C120
15	A6-B9-C121	A6-B9-C122	A6-B9-C123	A6-B9-C124	A6-B9-C125	A6-B9-C126
	A6-B9-C127	A6-B9-C128	A6-B9-C129	A6-B9-C130	A6-B9-C131	A6-B9-C132
	A6-B9-C133	A6-B9-C134	A6-B9-C135	A6-B9-C136	A6-B9-C137	A6-B9-C138
	A6-B9-C139	A6-B9-C140	BLANK	BLANK	BLANK	BLANK
	A6-B10-C1	A6-B10-C2	A6-B10-C3	A6-B10-C4	A6-B10-C5	A6-B10-C6
20	A6-B10-C7	A6-B10-C8	A6-B10-C9	A6-B10-C10	A6-B10-C11	A6-B10-C12
	A6-B10-C13	A6-B10-C14	A6-B10-C15	A6-B10-C16	A6-B10-C17	A6-B10-C18
	A6-B10-C19	A6-B10-C20	A6-B10-C21	A6-B10-C22	A6-B10-C23	A6-B10-C24
	A6-B10-C25	A6-B10-C26	A6-B10-C27	A6-B10-C28	A6-B10-C29	A6-B10-C30
	A6-B10-C31	A6-B10-C32	A6-B10-C33	A6-B10-C34	A6-B10-C35	A6-B10-C36
25	A6-B10-C37	A6-B10-C38	A6-B10-C39	A6-B10-C40	A6-B10-C41	A6-B10-C42
	A6-B10-C43	A6-B10-C44	A6-B10-C45	A6-B10-C46	A6-B10-C47	A6-B10-C48
	A6-B10-C49	A6-B10-C50	A6-B10-C51	A6-B10-C52	A6-B10-C53	A6-B10-C54
	A6-B10-C55	A6-B10-C56	A6-B10-C57	A6-B10-C58	A6-B10-C59	A6-B10-C60
	A6-B10-C61	A6-B10-C62	A6-B10-C63	A6-B10-C64	A6-B10-C65	A6-B10-C66
30	A6-B10-C67	A6-B10-C68	A6-B10-C69	A6-B10-C70	A6-B10-C71	A6-B10-C72
	A6-B10-C73	A6-B10-C74	A6-B10-C75	A6-B10-C76	A6-B10-C77	A6-B10-C78
	A6-B10-C79	A6-B10-C80	A6-B10-C81	A6-B10-C82	A6-B10-C83	A6-B10-C84
	A6-B10-C85	A6-B10-C86	A6-B10-C87	A6-B10-C88	A6-B10-C89	A6-B10-C90
	A6-B10-C91	A6-B10-C92	A6-B10-C93	A6-B10-C94	A6-B10-C95	A6-B10-C96
35	A6-B10-C97	A6-B10-C98	A6-B10-C99	A6-B10-C100	A6-B10-C101	A6-B10-C102
	A6-B10-C103	A6-B10-C104	A6-B10-C105	A6-B10-C106	A6-B10-C107	A6-B10-C108
	A6-B10-C109	A6-B10-C110	A6-B10-C111	A6-B10-C112	A6-B10-C113	A6-B10-C114

	A6-B10-C115	A6-B10-C116	A6-B10-C117	A6-B10-C118	A6-B10-C119	A6-B10-C120
	A6-B10-C121	A6-B10-C122	A6-B10-C123	A6-B10-C124	A6-B10-C125	A6-B10-C126
	A6-B10-C127	A6-B10-C128	A6-B10-C129	A6-B10-C130	A6-B10-C131	A6-B10-C132
	A6-B10-C133	A6-B10-C134	A6-B10-C135	A6-B10-C136	A6-B10-C137	A6-B10-C138
5	A6-B10-C139	A6-B10-C140	BLANK	BLANK	BLANK	BLANK
	A6-B11-C1	A6-B11-C2	A6-B11-C3	A6-B11-C4	A6-B11-C5	A6-B11-C6
	A6-B11-C7	A6-B11-C8	A6-B11-C9	A6-B11-C10	A6-B11-C11	A6-B11-C12
	A6-B11-C13	A6-B11-C14	A6-B11-C15	A6-B11-C16	A6-B11-C17	A6-B11-C18
	A6-B11-C19	A6-B11-C20	A6-B11-C21	A6-B11-C22	A6-B11-C23	A6-B11-C24
10	A6-B11-C25	A6-B11-C26	A6-B11-C27	A6-B11-C28	A6-B11-C29	A6-B11-C30
	A6-B11-C31	A6-B11-C32	A6-B11-C33	A6-B11-C34	A6-B11-C35	A6-B11-C36
	A6-B11-C37	A6-B11-C38	A6-B11-C39	A6-B11-C40	A6-B11-C41	A6-B11-C42
	A6-B11-C43	A6-B11-C44	A6-B11-C45	A6-B11-C46	A6-B11-C47	A6-B11-C48
	A6-B11-C49	A6-B11-C50	A6-B11-C51	A6-B11-C52	A6-B11-C53	A6-B11-C54
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	A6-B11-C61	A6-B11-C62	A6-B11-C63	A6-B11-C64	A6-B11-C65	A6-B11-C66
	A6-B11-C67	A6-B11-C68	A6-B11-C69	A6-B11-C70	A6-B11-C71	A6-B11-C72
	A6-B11-C73	A6-B11-C74	A6-B11-C75	A6-B11-C76	A6-B11-C77	A6-B11-C78
	A6-B11-C79	A6-B11-C80	A6-B11-C81	A6-B11-C82	A6-B11-C83	A6-B11-C84
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	A6-B11-C91	A6-B11-C92	A6-B11-C93	A6-B11-C94	A6-B11-C95	A6-B11-C96
	A6-B11-C97	A6-B11-C98	A6-B11-C99	A6-B11-C100	A6-B11-C101	A6-B11-C102
	A6-B11-C103	A6-B11-C104	A6-B11-C105	A6-B11-C106	A6-B11-C107	A6-B11-C108
	A6-B11-C109	A6-B11-C110	A6-B11-C111	A6-B11-C112	A6-B11-C113	A6-B11-C114
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	A6-B11-C121	A6-B11-C122	A6-B11-C123	A6-B11-C124	A6-B11-C125	A6-B11-C126
	A6-B11-C127	A6-B11-C128	A6-B11-C129	A6-B11-C130	A6-B11-C131	A6-B11-C132
	A6-B11-C133	A6-B11-C134	A6-B11-C135	A6-B11-C136	A6-B11-C137	A6-B11-C138
	A6-B11-C139	A6-B11-C140	BLANK	BLANK	BLANK	BLANK
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	A6-B12-C7	A6-B12-C8	A6-B12-C9	A6-B12-C10	A6-B12-C11	A6-B12-C12
	A6-B12-C13	A6-B12-C14	A6-B12-C15	A6-B12-C16	A6-B12-C17	A6-B12-C18
	A6-B12-C19	A6-B12-C20	A6-B12-C21	A6-B12-C22	A6-B12-C23	A6-B12-C24
	A6-B12-C25	A6-B12-C26	A6-B12-C27	A6-B12-C28	A6-B12-C29	A6-B12-C30
35	A6-B12-C31	A6-B12-C32	A6-B12-C33	A6-B12-C34	A6-B12-C35	A6-B12-C36
	A6-B12-C37	A6-B12-C38	A6-B12-C39	A6-B12-C40	A6-B12-C41	A6-B12-C42
	A6-B12-C43	A6-B12-C44	A6-B12-C45	A6-B12-C46	A6-B12-C47	A6-B12-C48

	A6-B12-C49	A6-B12-C50	A6-B12-C51	A6-B12-C52	A6-B12-C53	A6-B12-C54
	A6-B12-C55	A6-B12-C56	A6-B12-C57	A6-B12-C58	A6-B12-C59	A6-B12-C60
	A6-B12-C61	A6-B12-C62	A6-B12-C63	A6-B12-C64	A6-B12-C65	A6-B12-C66
	A6-B12-C67	A6-B12-C68	A6-B12-C69	A6-B12-C70	A6-B12-C71	A6-B12-C72
5	A6-B12-C73	A6-B12-C74	A6-B12-C75	A6-B12-C76	A6-B12-C77	A6-B12-C78
	A6-B12-C79	A6-B12-C80	A6-B12-C81	A6-B12-C82	A6-B12-C83	A6-B12-C84
	A6-B12-C85	A6-B12-C86	A6-B12-C87	A6-B12-C88	A6-B12-C89	A6-B12-C90
	A6-B12-C91	A6-B12-C92	A6-B12-C93	A6-B12-C94	A6-B12-C95	A6-B12-C96
	A6-B12-C97	A6-B12-C98	A6-B12-C99	A6-B12-C100	A6-B12-C101	A6-B12-C102
10	A6-B12-C103	A6-B12-C104	A6-B12-C105	A6-B12-C106	A6-B12-C107	A6-B12-C108
	A6-B12-C109	A6-B12-C110	A6-B12-C111	A6-B12-C112	A6-B12-C113	A6-B12-C114
	A6-B12-C115	A6-B12-C116	A6-B12-C117	A6-B12-C118	A6-B12-C119	A6-B12-C120
	A6-B12-C121	A6-B12-C122	A6-B12-C123	A6-B12-C124	A6-B12-C125	A6-B12-C126
	A6-B12-C127	A6-B12-C128	A6-B12-C129	A6-B12-C130	A6-B12-C131	A6-B12-C132
15	A6-B12-C133	A6-B12-C134	A6-B12-C135	A6-B12-C136	A6-B12-C137	A6-B12-C138
	A6-B12-C139	A6-B12-C140	BLANK	BLANK	BLANK	BLANK
	A6-B13-C1	A6-B13-C2	A6-B13-C3	A6-B13-C4	A6-B13-C5	A6-B13-C6
	A6-B13-C7	A6-B13-C8	A6-B13-C9	A6-B13-C10	A6-B13-C11	A6-B13-C12
	A6-B13-C13	A6-B13-C14	A6-B13-C15	A6-B13-C16	A6-B13-C17	A6-B13-C18
20	A6-B13-C19	A6-B13-C20	A6-B13-C21	A6-B13-C22	A6-B13-C23	A6-B13-C24
	A6-B13-C25	A6-B13-C26	A6-B13-C27	A6-B13-C28	A6-B13-C29	A6-B13-C30
	A6-B13-C31	A6-B13-C32	A6-B13-C33	A6-B13-C34	A6-B13-C35	A6-B13-C36
	A6-B13-C37	A6-B13-C38	A6-B13-C39	A6-B13-C40	A6-B13-C41	A6-B13-C42
	A6-B13-C43	A6-B13-C44	A6-B13-C45	A6-B13-C46	A6-B13-C47	A6-B13-C48
25	A6-B13-C49	A6-B13-C50	A6-B13-C51	A6-B13-C52	A6-B13-C53	A6-B13-C54
•	A6-B13-C55	A6-B13-C56	A6-B13-C57	A6-B13-C58	A6-B13-C59	A6-B13-C60
	A6-B13-C61	A6-B13-C62	A6-B13-C63	A6-B13-C64	A6-B13-C65	A6-B13-C66
	A6-B13-C67	A6-B13-C68	A6-B13-C69	A6-B13-C70	A6-B13-C71	A6-B13-C72
	A6-B13-C73	A6-B13-C74	A6-B13-C75	A6-B13-C76	A6-B13-C77	A6-B13-C78
30	A6-B13-C79	A6-B13-C80	A6-B13-C81	A6-B13-C82	A6-B13-C83	A6-B13-C84
	A6-B13-C85	A6-B13-C86	A6-B13-C87	A6-B13-C88	A6-B13-C89	A6-B13-C90
	A6-B13-C91	A6-B13-C92	A6-B13-C93	A6-B13-C94	A6-B13-C95	A6-B13-C96
	A6-B13-C97	A6-B13-C98	A6-B13-C99	A6-B13-C100	A6-B13-C101	A6-B13-C102
	A6-B13-C103	A6-B13-C104	A6-B13-C105	A6-B13-C106	A6-B13-C107	A6-B13-C108
35	A6-B13-C109	A6-B13-C110	A6-B13-C111	A6-B13-C112	A6-B13-C113	A6-B13-C114
	A6-B13-C115	A6-B13-C116	A6-B13-C117	A6-B13-C118	A6-B13-C119	A6-B13-C120
	A6-B13-C121	A6-B13-C122	A6-B13-C123	A6-B13-C124	A6-B13-C125	A6-B13-C126

	A6-B13-C127	A6-B13-C128	A6-B13-C129	A6-B13-C130	A6-B13-C131	A6-B13-C132
	A6-B13-C133	A6-B13-C134	A6-B13-C135	A6-B13-C136	A6-B13-C137	A6-B13-C138
	A6-B13-C139	A6-B13-C140	BLANK	BLANK	BLANK	BLANK
	A7-B1-C1	A7-B1-C2	A7-B1-C3	A7-B1-C4	A7-B1-C5	A7-B1-C6
5	A7-B1-C7	A7-B1-C8	A7-B1-C9	A7-B1-C10	A7-B1-C11	A7-B1-C12
	A7-B1-C13	A7-B1-C14	A7-B1-C15	A7-B1-C16	A7-B1-C17	A7-B1-C18
	A7-B1-C19	A7-B1-C20	A7-B1-C21	A7-B1-C22	A7-B1-C23	A7-B1-C24
	A7-B1-C25	A7-B1-C26	A7-B1-C27	A7-B1-C28	A7-B1-C29	A7-B1-C30
	A7-B1-C31	A7-B1-C32	A7-B1-C33	A7-B1-C34	A7-B1-C35	A7-B1-C36
10	A7-B1-C37	A7-B1-C38	A7-B1-C39	A7-B1-C40	A7-B1-C41	A7-B1-C42
	A7-B1-C43	A7-B1-C44	A7-B1-C45	A7-B1-C46	A7-B1-C47	A7-B1-C48
	A7-B1-C49	A7-B1-C50	A7-B1-C51	A7-B1-C52	A7-B1-C53	A7-B1-C54
	A7-B1-C55	A7-B1-C56	A7-B1-C57	A7-B1-C58	A7-B1-C59	A7-B1-C60
	A7-B1-C61	A7-B1-C62	A7-B1-C63	A7-B1-C64	A7-B1-C65	A7-B1-C66
15	A7-B1-C67	A7-B1-C68	A7-B1-C69	A7-B1-C70	A7-B1-C71	A7-B1-C72
	A7-B1-C73	A7-B1-C74	A7-B1-C75	A7-B1-C76	A7-B1-C77	A7-B1-C78
	A7-B1-C79	A7-B1-C80	A7-B1-C81	A7-B1-C82	A7-B1-C83	A7-B1-C84
	A7-B1-C85	A7-B1-C86	A7-B1-C87	A7-B1-C88	A7-B1-C89	A7-B1-C90
	A7-B1-C91	A7-B1-C92	A7-B1-C93	A7-B1-C94	A7-B1-C95	A7-B1-C96
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	A7-B1-C103	A7-B1-C104	A7-B1-C105	A7-B1-C106	A7-B1-C107	A7-B1-C108
	A7-B1-C109	A7-B1-C110	A7-B1-C111	A7-B1-C112	A7-B1-C113	A7-B1-C114
	A7-B1-C115	A7-B1-C116	A7-B1-C117	A7-B1-C118	A7-B1-C119	A7-B1-C120
	A7-B1-C121	A7-B1-C122	A7-B1-C123	A7-B1-C124	A7-B1-C125	A7-B1-C126
25	A7-B1-C127	A7-B1-C128	A7-B1-C129	A7-B1-C130	A7-B1-C131	A7-B1-C132
	A7-B1-C133	A7-B1-C134	A7-B1-C135	A7-B1-C136	A7-B1-C137	A7-B1-C138
	A7-B1-C139	A7-B1-C140	BLANK	BLANK	BLANK	BLANK
	A7-B2-C1	A7-B2-C2	A7-B2-C3	A7-B2-C4	A7-B2-C5	A7-B2-C6
	A7-B2-C7	A7-B2-C8	A7-B2-C9	A7-B2-C10	A7-B2-C11	A7-B2-C12
30	A7-B2-C13	A7-B2-C14	A7-B2-C15	A7-B2-C16	A7-B2-C17	A7-B2-C18
	A7-B2-C19	A7-B2-C20	A7-E2-C21	A7-B2-C22	A7-B2-C23	A7-B2-C24
	A7-B2-C25	A7-B2-C26	A7-B2-C27	A7-B2-C28	A7-B2-C29	A7-B2-C30
	A7-B2-C31	A7-B2-C32	A7-B2-C33	A7-B2-C34	A7-B2-C35	A7-B2-C36
	A7-B2-C37	A7-B2-C38	A7-B2-C39	A7-B2-C40	A7-B2-C41	A7-B2-C42
35	A7-B2-C43	A7-B2-C44	A7-B2-C45	A7-B2-C46	A7-B2-C47	A7-B2-C48
	A7-B2-C49	A7-B2-C50	A7-B2-C51	A7-B2-C52	A7-B2-C53	A7-B2-C54
	A7-B2-C55	A7-B2-C56	A7-B2-C57	A7-B2-C58	A7-B2-C59	A7-B2-C60

	A7-B2-C61	A7-B2-C62	A7-B2-C63	A7-B2-C64	A7-B2-C65	A7-B2-C66
	A7-B2-C67	A7-B2-C68	A7-B2-C69	A7-B2-C70	A7-B2-C71	A7-B2-C72
	A7-B2-C73	A7-B2-C74	A7-B2-C75	A7-B2-C76	A7-B2-C77	A7-B2-C78
	A7-B2-C79	A7-B2-C80	A7-B2-C81	A7-B2-C82	A7-B2-C83	A7-B2-C84
5	A7-B2-C85	A7-B2-C86	A7-B2-C87	A7-B2-C88	A7-B2-C89	A7-B2-C90
	A7-B2-C91	A7-B2-C92	A7-B2-C93	A7-B2-C94	A7-B2-C95	A7-B2-C96
	A7-B2-C97	A7-B2-C98	A7-B2-C99	A7-B2-C100	A7-B2-C101	A7-B2-C102
	A7-B2-C103	A7-B2-C104	A7-B2-C105	A7-B2-C106	A7-B2-C107	A7-B2-C108
	A7-B2-C109	A7-B2-C110	A7-B2-C111	A7-B2-C112	A7-B2-C113	A7-B2-C114
10	A7-B2-C115	A7-B2-C116	A7-B2-C117	A7-B2-C118	A7-B2-C119	A7-B2-C120
	A7-B2-C121	A7-B2-C122	A7-B2-C123	A7-B2-C124	A7-B2-C125	A7-B2-C126
	A7-B2-C127	A7-B2-C128	A7-B2-C129	A7-B2-C130	A7-B2-C131	A7-B2-C132
	A7-B2-C133	A7-B2-C134	A7-B2-C135	A7-B2-C136	A7-B2-C137	A7-B2-C138
	A7-B2-C139	A7-B2-C140	BLANK	BLANK	BLANK	BLANK
15	A7-B3-C1	A7-B3-C2	A7-B3-C3	A7-B3-C4	A7-B3-C5	A7-B3-C6
	A7-B3-C7	A7-B3-C8	A7-B3-C9	A7-B3-C10	A7-B3-C11	A7-B3-C12
	A7-B3-C13	A7-B3-C14	A7-B3-C15	A7-B3-C16	A7-B3-C17	A7-B3-C18
	A7-B3-C19	A7-B3-C20	A7-B3-C21	A7-B3-C22	A7-B3-C23	A7-B3-C24
	A7-B3-C25	A7-B3-C26	A7-B3-C27	A7-B3-C28	A7-B3-C29	A7-B3-C30
20	A7-B3-C31	A7-B3-C32	A7-B3-C33	A7-B3-C34	A7-B3-C35	A7-B3-C36
	A7-B3-C37	A7-B3-C38	A7-B3-C39	A7-B3-C40	A7-B3-C41	A7-B3-C42
	A7-B3-C43	A7-B3-C44	A7-B3-C45	A7-B3-C46	A7-B3-C47	A7-B3-C48
	A7-B3-C49	A7-B3-C50	A7-B3-C51	A7-B3-C52	A7-B3-C53	A7-B3-C54
	A7-B3-C55	A7-B3-C56	A7-B3-C57	A7-B3-C58	A7-B3-C59	A7-B3-C60
25	A7-B3-C61	A7-B3-C62	A7-B3-C63	A7-B3-C64	A7-B3-C65	A7-B3-C66
	A7-B3-C67	A7-B3-C68	A7-B3-C69	A7-B3-C70	A7-B3-C71	A7-B3-C72
	A7-B3-C73	A7-B3-C74	A7-B3-C75	A7-B3-C76	A7-B3-C77	A7-B3-C78
	A7-B3-C79	A7-B3-C80	A7-B3-C81	A7-B3-C82	A7-B3-C83	A7-B3-C84
	A7-B3-C85	A7-B3-C86	A7-B3-C87	A7-B3-C88	A7-B3-C89	A7-B3-C90
30	A7-B3-C91	A7-B3-C92	A7-B3-C93	A7-B3-C94	A7-B3-C95	A7-B3-C96
	A7-B3-C97	A7-B3-C98	A7-B3-C99	A7-B3-C100	A7-B3-C101	A7-B3-C102
	A7-B3-C103	A7-B3-C104	A7-B3-C105	A7-B3-C106	A7-B3-C107	A7-B3-C108
	A7-B3-C109	A7-B3-C110	A7-B3-C111	A7-B3-C112	A7-B3-C113	A7-B3-C114
	A7-B3-C115	A7-B3-C116	A7-B3-C117	A7-B3-C118	A7-B3-C119	A7-B3-C120
35	A7-B3-C121	A7-B3-C122	A7-B3-C123	A7-B3-C124	A7-B3-C125	A7-B3-C126
	A7-B3-C127	A7-B3-C128	A7-B3-C129	A7-B3-C130	A7-B3-C131	A7-B3-C132
	A7-B3-C133	A7-B3-C134	A7-B3-C135	A7-B3-C136	A7-B3-C137	A7-B3-C138

	A7-B3-C139	A7-B3-C140	BLANK	BLANK	BLANK	BLANK
	A7-B4-C1	A7-B4-C2	A7-B4-C3	A7-B4-C4	A7-B4-C5	A7-B4-C6
	A7-B4-C7	A7-B4-C8	A7-B4-C9	A7-B4-C10	A7-B4-C11	A7-B4-C12
	A7-B4-C13	A7-B4-C14	A7-B4-C15	A7-B4-C16	A7-B4-C17	A7-B4-C18
5	A7-B4-C19	A7-B4-C20	A7-B4-C21	A7-B4-C22	A7-B4-C23	A7-B4-C24
	A7-B4-C25	A7-B4-C26	A7-B4-C27	A7-B4-C28	A7-B4-C29	A7-B4-C30
	A7-B4-C31	A7-B4-C32	A7-B4-C33	A7-B4-C34	A7-B4-C35	A7-B4-C36
	A7-B4-C37	A7-B4-C38	A7-B4-C39	A7-B4-C40	A7-B4-C41	A7-B4-C42
	A7-B4-C43	A7-B4-C44	A7-B4-C45	A7-B4-C46	A7-B4-C47	A7-B4-C48
10	A7-B4-C49	A7-B4-C50	A7-B4-C51	A7-B4-C52	A7-B4-C53	A7-B4-C54
	A7-B4-C55	A7-B4-C56	A7-B4-C57	A7-B4-C58	A7-B4-C59	A7-B4-C60
	A7-B4-C61	A7-B4-C62	A7-B4-C63	A7-B4-C64	A7-B4-C65	A7-B4-C66
	A7-B4-C67	A7-B4-C68	A7-B4-C69	A7-B4-C70	A7-B4-C71	A7-B4-C72
	A7-B4-C73	A7-B4-C74	A7-B4-C75	A7-B4-C76	A7-B4-C77	A7-B4-C78
15	A7-B4-C79	A7-B4-C80	A7-B4-C81	A7-B4-C82	A7-B4-C83	A7-B4-C84
	A7-B4-C85	A7-B4-C86	A7-B4-C87	A7-B4-C88	A7-B4-C89	A7-B4-C90
	A7-B4-C91	A7-B4-C92	A7-B4-C93	A7-B4-C94	A7-B4-C95	A7-B4-C96
	A7-B4-C97	A7-B4-C98	A7-B4-C99	A7-B4-C100	A7-B4-C101	A7-B4-C102
	A7-B4-C103	A7-B4-C104	A7-B4-C105	A7-B4-C106	A7-B4-C107	A7-B4-C108
20	A7-B4-C109	A7-B4-C110	A7-B4-C111	A7-B4-C112	A7-B4-C113	A7-B4-C114
	A7-B4-C115	A7-B4-C116	A7-B4-C117	A7-B4-C118	A7-B4-C119	A7-B4-C120
	A7-B4-C121	A7-B4-C122	A7-B4-C123	A7-B4-C124	A7-B4-C125	A7-B4-C126
	A7-B4-C127	A7-B4-C128	A7-B4-C129	A7-B4-C130	A7-B4-C131	A7-B4-C132
	A7-B4-C133	A7-B4-C134	A7-B4-C135	A7-B4-C136	A7-B4-C137	A7-B4-C138
25	A7-B4-C139	A7-B4-C140	BLANK	BLANK	BLANK	BLANK
	A7-B5-C1	A7-B5-C2	A7-B5-C3	A7-B5-C4	A7-B5-C5	A7-B5-C6
	A7-B5-C7	A7-B5-C8	A7-B5-C9	A7-B5-C10	A7-B5-C11	A7-B5-C12
	A7-B5-C13	A7-B5-C14	A7-B5-C15	A7-B5-C16	A7-B5-C17	A7-B5-C18
	A7-B5-C19	A7-B5-C20	A7-B5-C21	A7-B5-C22	A7-B5-C23	A7-B5-C24
30	A7-B5-C25	A7-B5-C26	A7-B5-C27	A7-B5-C28	A7-B5-C29	A7-B5-C30
	A7-B5-C31	A7-B5-C32	A7-B5-C33	A7-B5-C34	A7-B5-C35	A7-B5-C36
	A7-B5-C37	A7-B5-C38	A7-B5-C39	A7-B5-C40	A7-B5-C41	A7-B5-C42
	A7-B5-C43	A7-B5-C44	A7-B5-C45	A7-B5-C46	A7-B5-C47	A7-B5-C48
	A7-B5-C49	A7-B5-C50	A7-B5-C51	A7-B5-C52	A7-B5-C53	A7-B5-C54
35	A7-B5-C55	A7-B5-C56	A7-B5-C57	A7-B5-C58	A7-B5-C59	A7-B5-C60
	A7-B5-C61	A7-B5-C62	A7-B5-C63	A7-B5-C64	A7-B5-C65	A7-B5-C66
	A7-B5-C67	A7-B5-C68	A7-B5-C69	A7-B5-C70	A7-B5-C71	A7-B5-C72

	A7-B5-C73	A7-B5-C74	A7-B5-C75	A7-B5-C76	A7-B5-C77	A7-B5-C78
	A7-B5-C79	A7-B5-C80	A7-B5-C81	A7-B5-C82	A7-B5-C83	A7-B5-C84
	A7-B5-C85	A7-B5-C86	A7-B5-C87	A7-B5-C88	A7-B5-C89	A7-B5-C90
	A7-B5-C91	A7-B5-C92	A7-B5-C93	A7-B5-C94	A7-B5-C95	A7-B5-C96
5	A7-B5-C97	A7-B5-C98	A7-B5-C99	A7-B5-C100	A7-B5-C101	A7-B5-C102
	A7-B5-C103	A7-B5-C104	A7-B5-C105	A7-B5-C106	A7-B5-C107	A7-B5-C108
	A7-B5-C109	A7-B5-C110	A7-B5-C111	A7-B5-C112	A7-B5-C113	A7-B5-C114
	A7-B5-C115	A7-B5-C116	A7-B5-C117	A7-B5-C118	A7-B5-C119	A7-B5-C120
	A7-B5-C121	A7-B5-C122	A7-B5-C123	A7-B5-C124	A7-B5-C125	A7-B5-C126
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	A7-B5-C139	A7-B5-C140	BLANK	BLANK	BLANK	BLANK
	A7-B6-C1	A7-B6-C2	A7-B6-C3	A7-B6-C4	A7-B6-C5	A7-B6-C6
	A7-B6-C7	A7-B6-C8	A7-B6-C9	A7-B6-C10	A7-B6-C11	A7-B6-C12
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	A7-B6-C19	A7-B6-C20	A7-B6-C21	A7-B6-C22	A7-B6-C23	A7-B6-C24
	A7-B6-C25	A7-B6-C26	A7-B6-C27	A7-B6-C28	A7-B6-C29	A7-B6-C30
	A7-B6-C31	A7-B6-C32	A7-B6-C33	A7-B6-C34	A7-B6-C35	A7-B6-C36
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20 ·	A7-B6-C43	A7-B6-C44	A7-B6-C45	A7-B6-C46	A7-B6-C47	A7-B6-C48
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	A7-B6-C139	A7-B6-C140	BLANK	BLANK	BLANK	BLANK
	A7-B7-C1	A7-B7-C2	A7-B7-C3	A7-B7-C4	A7-B7-C5	A7-B7-C6

87

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	A7-B7-C139	A7-B7-C140	BLANK	BLANK	BLANK	BLANK
	A7-B8-C1	A7-B8-C2	A7-B8-C3	A7-B8-C4	A7-B8-C5	A7-B8-C6
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	A7-B8-C97	A7-B8-C98	A7-B8-C99	A7-B8-C100	A7-B8-C101	A7-B8-C102
	A7-B8-C103	A7-B8-C104	A7-B8-C105	A7-B8-C106	A7-B8-C107	A7-B8-C108
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	A7-B8-C133	A7-B8-C134	A7-B8-C135	A7-B8-C136	A7-B8-C137	A7-B8-C138
10	A7-B8-C139	A7-B8-C140	BLANK	BLANK	BLANK	BLANK
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	A7-B9-C43	A7-B9-C44	A7-B9-C45	A7-B9-C46	A7-B9-C47	A7-B9-C48
	A7-B9-C49	A7-B9-C50	A7-B9-C51	A7-B9-C52	A7-B9-C53	A7-B9-C54
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	A7-B9-C103	A7-B9-C104	A7-B9-C105	A7-B9-C106	A7-B9-C107	A7-B9-C108
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	A7-B9-C127	A7-B9-C128	A7-B9-C129	A7-B9-C130	A7-B9-C131	A7-B9-C132
	A7-B9-C133	A7-B9-C134	A7-B9-C135	A7-B9-C136	A7-B9-C137	A7-B9-C138
	A7-B9-C139	A7-B9-C140	BLANK	BLANK	BLANK	BLANK
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	A7-B10-C7	A7-B10-C8	A7-B10-C9	A7-B10-C10	A7-B10-C11	A7-B10-C12
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	A7-B10-C139	A7-B10-C140	BLANK	BLANK	BLANK	BLANK
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	A7-B11-C127	A7-B11-C128	A7-B11-C129	A7-B11-C130	A7-B11-C131	A7-B11-C132
	A7-B11-C133	A7-B11-C134	A7-B11-C135	A7-B11-C136	A7-B11-C137	A7-B11-C138
	A7-B11-C139	A7-B11-C140	BLANK	BLANK	BLANK	BLANK
	A7-B12-C1	A7-B12-C2	A7-B12-C3	A7-B12-C4	A7-B12-C5	A7-B12-C6
10	A7-B12-C7	A7-B12-C8	A7-B12-C9	A7-B12-C10	A7-B12-C11	A7-B12-C12
	A7-B12-C13	A7-B12-C14	A7-B12-C15	A7-B12-C16	A7-B12-C17	A7-B12-C18
	A7-B12-C19	A7-B12-C20	A7-B12-C21	A7-B12-C22	A7-B12-C23	A7-B12-C24
	A7-B12-C25	A7-B12-C26	A7-B12-C27	A7-B12-C28	A7-B12-C29	A7-B12-C30
	A7-B12-C31	A7-B12-C32	A7-B12-C33	A7-B12-C34	A7-B12-C35	A7-B12-C36
15	A7-B12-C37	A7-B12-C38	A7-B12-C39	A7-B12-C40	A7-B12-C41	A7-B12-C42
	A7-B12-C43	A7-B12-C44	A7-B12-C45	A7-B12-C46	A7-B12-C47	A7-B12-C48
	A7-B12-C49	A7-B12-C50	A7-B12-C51	A7-B12-C52	A7-B12-C53	A7-B12-C54
	A7-B12-C55	A7-B12-C56	A7-B12-C57	A7-B12-C58	A7-B12-C59	A7-B12-C60
	A7-B12-C61	A7-B12-C62	A7-B12-C63	A7-B12-C64	A7-B12-C65	A7-B12-C66
20	A7-B12-C67	A7-B12-C68	A7-B12-C69	A7-B12-C70	A7-B12-C71	A7-B12-C72
	A7-B12-C73	A7-B12-C74	A7-B12-C75	A7-B12-C76	A7-B12-C77	A7-B12-C78
•	A7-B12-C79	A7-B12-C80	A7-B12-C81	A7-B12-C82	A7-B12-C83	A7-B12-C84
	A7-B12-C85	A7-B12-C86	A7-B12-C87	A7-B12-C88	A7-B12-C89	A7-B12-C90
	A7-B12-C91	A7-B12-C92	A7-B12-C93	A7-B12-C94	A7-B12-C95	A7-B12-C96
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	A7-B12-C103	A7-B12-C104	A7-B12-C105	A7-B12-C106	A7-B12-C107	A7-B12-C108
	A7-B12-C109	A7-B12-C110	A7-B12-C111	A7-B12-C112	A7-B12-C113	A7-B12-C114
	A7-B12-C115	A7-B12-C116	A7-B12-C117	A7-B12-C118	A7-B12-C119	A7-B12-C120
	A7-B12-C121	A7-B12-C122	A7-B12-C123	A7-B12-C124	A7-B12-C125	A7-B12-C126
30	A7-B12-C127	A7-B12-C128	A7-B12-C129	A7-B12-C130	A7-B12-C131	A7-B12-C132
	A7-B12-C133	A7-B12-C134	A7-B12-C135	A7-B12-C136	A7-B12-C137	A7-B12-C138
	A7-B12-C139	A7-B12-C140	BLANK	BLANK	BLANK	BLANK
	A7-B13-C1	A7-B13-C2	A7-B13-C3	A7-B13-C4	A7-B13-C5	A7-B13-C6
	A7-B13-C7	A7-B13-C8	A7-B13-C9	A7-B13-C10	A7-B13-C11	A7-B13-C12
35	A7-B13-C13	A7-B13-C14	A7-B13-C15	A7-B13-C16	A7-B13-C17	A7-B13-C18
	A7-B13-C19	A7-B13-C20	A7-B13-C21	A7-B13-C22	A7-B13-C23	A7-B13-C24
	A7-B13-C25	A7-B13-C26	A7-B13-C27	A7-B13-C28	A7-B13-C29	A7-B13-C30

	A7-B13-C31	A7-B13-C32	A7-B13-C33	A7-B13-C34	A7-B13-C35	A7-B13-C36
	A7-B13-C37	A7-B13-C38	A7-B13-C39	A7-B13-C40	A7-B13-C41	A7-B13-C42
	A7-B13-C43	A7-B13-C44	A7-B13-C45	A7-B13-C46	.A7-B13-C47	A7-B13-C48
	A7-B13-C49	A7-B13-C50	A7-B13-C51	A7-B13-C52	A7-B13-C53	A7-B13-C54
5	A7-B13-C55	A7-B13-C56	A7-B13-C57	A7-B13-C58	A7-B13-C59	A7-B13-C60
	A7-B13-C61	A7-B13-C62	A7-B13-C63	A7-B13-C64	A7-B13-C65	A7-B13-C66
	A7-B13-C67	A7-B13-C68	A7-B13-C69	A7-B13-C70	A7-B13-C71	A7-B13-C72
	A7-B13-C73	A7-B13-C74	A7-B13-C75	A7-B13-C76	A7-B13-C77	A7-B13-C78
	A7-B13-C79	A7-B13-C80	A7-B13-C81	A7-B13-Ç82	A7-B13-C83	A7-B13-C84
10	A7-B13-C85	A7-B13-C86	A7-B13-C87	A7-B13-C88	A7-B13-C89	A7-B13-C90
	A7-B13-C91	A7-B13-C92	A7-B13-C93	A7-B13-C94	A7-B13-C95	A7-B13-C96
	A7-B13-C97	A7-B13-C98	A7-B13-C99	A7-B13-C100	A7-B13-C101	A7-B13-C102
	A7-B13-C103	A7-B13-C104	A7-B13-C105	A7-B13-C106	A7-B13-C107	A7-B13-C108
	A7-B13-C109	A7-B13-C110	A7-B13-C111	A7-B13-C112	A7-B13-C113	A7-B13-C114
15	A7-B13-C115	A7-B13-C116	A7-B13-C117	A7-B13-C118	A7-B13-C119	A7-B13-C120
	A7-B13-C121	A7-B13-C122	A7-B13-C123	A7-B13-C124	A7-B13-C125	A7-B13-C126
	A7-B13-C127	A7-B13-C128	A7-B13-C129	A7-B13-C130	A7-B13-C131	A7-B13-C132
	A7-B13-C133	A7-B13-C134	A7-B13-C135	A7-B13-C136	A7-B13-C137	A7-B13-C138
	A7-B13-C139	A7-B13-C140	BLANK	BLANK	BLANK	BLANK
20	A8-B1-C1	A8-B1-C2	A8-B1-C3	A8-B1-C4	A8-B1-C5	A8-B1-C6
	A8-B1-C7	A8-B1-C8	A8-B1-C9	A8-B1-C10	A8-B1-C11	A8-B1-C12
	A8-B1-C13	A8-B1-C14	A8-B1-C15	A8-B1-C16	A8-B1-C17	A8-B1-C18
	A8-B1-C19	A8-B1-C20	A8-B1-C21	A8-B1-C22	A8-B1-C23	A8-B1-C24
	A8-B1-C25	A8-B1-C26	A8-B1-C27	A8-B1-C28	A8-B1-C29	A8-B1-C30
25	A8-B1-C31	A8-B1-C32	A8-B1-C33	A8-B1-C34	A8-B1-C35	A8-B1-C36
	A8-B1-C37	A8-B1-C38	A8-B1-C39	A8-B1-C40	A8-B1-C41	A8-B1-C42
	A8-B1-C43	A8-B1-C44	A8-B1-C45	A8-B1-C46	A8-B1-C47	A8-B1-C48
	A8-B1-C49	A8-B1-C50	A8-B1-C51	A8-B1-C52	A8-B1-C53	A8-B1-C54
	A8-B1-C55	A8-B1-C56	A8-B1-C57	A8-B1-C58	A8-B1-C59	A8-B1-C60
30	A8-B1-C61	A8-B1-C62	A8-B1-C63	A8-B1-C64	A8-B1-C65	A8-B1-C66
	A8-B1-C67	A8-B1-C68	A8-B1-C69	A8-B1-C70	A8-B1-C71	A8-B1-C72
	A8-B1-C73	A8-B1-C74	A8-B1-C75	A8-B1-C76	A8-B1-C77	A8-B1-C78
	A8-B1-C79	A8-B1-C80	A8-B1-C81	A8-B1-C82	A8-B1-C83	A8-B1-C84
	A8-B1-C85	A8-B1-C86	A8-B1-C87	A8-B1-C88	A8-B1-C89	A8-B1-C90
35	A8-B1-C91	A8-B1-C92	A8-B1-C93	A8-B1-C94	A8-B1-C95	A8-B1-C96
	A8-B1-C97	A8-B1-C98	A8-B1-C99	A8-B1-C100	A8-B1-C101	A8-B1-C102
	A8-B1-C103	A8-B1-C104	A8-B1-C105	A8-B1-C106	A8-B1-C107	A8-B1-C108

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	A8-B1-C109	A8-B1-C110	A8-B1-C111	A8-B1-C112	A8-B1-C113	A8-B1-C114
	A8-B1-C115	A8-B1-C116	A8-B1-C117	A8-B1-C118	A8-B1-C119	A8-B1-C120
	A8-B1-C121	A8-B1-C122	A8-B1-C123	A8-B1-C124	A8-B1-C125	A8-B1-C126
	A8-B1-C127	A8-B1-C128	A8-B1-C129	A8-B1-C130	A8-B1-C131	A8-B1-C132
5	A8-B1-C133	A8-B1-C134	A8-B1-C135	A8-B1-C136	A8-B1-C137	A8-B1-C138
	A8-B1-C139	A8-B1-C140	BLANK	BLANK	BLANK	BLANK
	A8-B2-C1	A8-B2-C2	A8-B2-C3	A8-B2-C4	A8-B2-C5	A8-B2-C6
	A8-B2-C7	A8-B2-C8	A8-B2-C9	A8-B2-C10	A8-B2-C11	A8-B2-C12
	A8-B2-C13	A8-B2-C14	A8-B2-C15	A8-B2-C16	A8-B2-C17	A8-B2-C18
10	A8-B2-C19	A8-B2-C20	A8-B2-C21	A8-B2-C22	A8-B2-C23	A8-B2-C24
	A8-B2-C25	A8-B2-C26	A8-B2-C27	A8-B2-C28	A8-B2-C29	A8-B2-C30
	A8-B2-C31	A8-B2-C32	A8-B2-C33	A8-B2-C34	A8-B2-C35	A8-B2-C36
	A8-B2-C37	A8-B2-C38	A8-B2-C39	A8-B2-C40	A8-B2-C41	A8-B2-C42
	A8-B2-C43	A8-B2-C44	A8-B2-C45	A8-B2-C46	A8-B2-C47	A8-B2-C48
15	A8-B2-C49	A8-B2-C50	A8-B2-C51	A8-B2-C52	A8-B2-C53	A8-B2-C54
	A8-B2-C55	A8-B2-C56	A8-B2-C57	A8-B2-C58	A8-B2-C59	A8-B2-C60
	A8-B2-C61	A8-B2-C62	A8-B2-C63	A8-B2-C64	A8-B2-C65	A8-B2-C66
	A8-B2-C67	A8-B2-C68	A8-B2-C69	A8-B2-C70	A8-B2-C71	A8-B2-C72
	A8-B2-C73	A8-B2-C74	A8-B2-C75	A8-B2-C76	A8-B2-C77	A8-B2-C78
20	A8-B2-C79	A8-B2-C80	A8-B2-C81	A8-B2-C82	A8-B2-C83	A8-B2-C84
	A8-B2-C85	A8-B2-C86	A8-B2-C87	A8-B2-C88	A8-B2-C89	A8-B2-C90
	A8-B2-C91	A8-B2-C92	A8-B2-C93	A8-B2-C94	A8-B2-C95	A8-B2-C96
	A8-B2-C97	A8-B2-C98	A8-B2-C99	A8-B2-C100	A8-B2-C101	A8-B2-C102
	A8-B2-C103	A8-B2-C104	A8-B2-C105	A8-B2-C106	A8-B2-C107	A8-B2-C108
25	A8-B2-C109	A8-B2-C110	A8-B2-C111	A8-B2-C112	A8-B2-C113	A8-B2-C114
	A8-B2-C115	A8-B2-C116	A8-B2-C117	A8-B2-C118	A8-B2-C119	A8-B2-C120
	A8-B2-C121	A8-B2-C122	A8-B2-C123	A8-B2-C124	A8-B2-C125	A8-B2-C126
	A8-B2-C127	A8-B2-C128	A8-B2-C129	A8-B2-C130	A8-B2-C131	A8-B2-C132
	A8-B2-C133	A8-B2-C134	A8-B2-C135	A8-B2-C136	A8-B2-C137	A8-B2-C138
30	A8-B2-C139	A8-B2-C140	BLANK	BLANK	BLANK	BLANK
	A8-B3-C1	A8-B3-C2	A8-B3-C3	A8-B3-C4	A8-B3-C5	A8-B3-C6
	A8-B3-C7	A8-B3-C8	A8-B3-C9	A8-B3-C10	A8-B3-C11	A8-B3-C12
	A8-B3-C13	A8-B3-C14	A8-B3-C15	A8-B3-C16	A8-B3-C17	A8-B3-C18
	A8-B3-C19	A8-B3-C20	A8-B3-C21	A8-B3-C22	A8-B3-C23	A8-B3-C24
35	A8-B3-C25	A8-B3-C26	A8-B3-C27	A8-B3-C28	A8-B3-C29	A8-B3-C30
	A8-B3-C31	A8-B3-C32	A8-B3-C33	A8-B3-C34	A8-B3-C35	A8-B3-C36
	A8-B3-C37	A8-B3-C38	A8-B3-C39	A8-B3-C40	A8-B3-C41	A8-B3-C42

	A8-B3-C43	A8-B3-C44	A8-B3-C45	A8-B3-C46	A8-B3-C47	A8-B3-C48
	A8-B3-C49	A8-B3-C50	A8-B3-C51	A8-B3-C52	A8-B3-C53	A8-B3-C54
	A8-B3-C55	A8-B3-C56	A8-B3-C57	A8-B3-C58	A8-B3-C59	A8-B3-C60
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	A8-B3-C91	A8-B3-C92	A8-B3-C93	A8-B3-C94	A8-B3-C95	A8-B3-C96
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	A8-B3-C103	A8-B3-C104	A8-B3-C105	A8-B3-C106	A8-B3-C107	A8-B3-C108
	A8-B3-C109	A8-B3-C110	A8-B3-C111	A8-B3-C112	A8-B3-C113	A8-B3-C114
	A8-B3-C115	A8-B3-C116	A8-B3-C117	A8-B3-C118	A8-B3-C119	A8-B3-C120
	A8-B3-C121	A8-B3-C122	A8-B3-C123	A8-B3-C124	A8-B3-C125	A8-B3-C126
15	A8-B3-C127	A8-B3-C128	A8-B3-C129	A8-B3-C130	A8-B3-C131	A8-B3-C132
	A8-B3-C133	A8-B3-C134	A8-B3-C135	A8-B3-C136	A8-B3-C137	A8-B3-C138
	A8-B3-C139	A8-B3-C140	BLANK	BLANK	BLANK	BLANK
	A8-B4-C1	A8-B4-C2	A8-B4-C3	A8-B4-C4	A8-B4-C5	A8-B4-C6
	A8-B4-C7	A8-B4-C8	A8-B4-C9	A8-B4-C10	A8-B4-C11	A8-B4-C12
20	A8-B4-C13	A8-B4-C14	A8-B4-C15	A8-B4-C16	A8-B4-C17	A8-B4-C18
	A8-B4-C19	A8-B4-C20	A8-B4-C21	A8-B4-C22	A8-B4-C23	A8-B4-C24
	A8-B4-C25	A8-B4-C26	A8-B4-C27	A8-B4-C28	A8-B4-C29	A8-B4-C30
	A8-B4-C31	A8-B4-C32	A8-B4-C33	A8-B4-C34	A8-B4-C35	A8-B4-C36
	A8-B4-C37	A8-B4-C38	A8-B4-C39	A8-B4-C40	A8-B4-C41	A8-B4-C42
25	A8-B4-C43	A8-B4-C44	A8-B4-C45	A8-B4-C46	A8-B4-C47	A8-B4-C48
	A8-B4-C49	A8-B4-C50	A8-B4-C51	A8-B4-C52	A8-B4-C53	A8-B4-C54
	A8-B4-C55	A8-B4-C56	A8-B4-C57	A8-B4-C58	A8-B4-C59	A8-B4-C60
	A8-B4-C61	A8-B4-C62	A8-B4-C63	A8-B4-C64	A8-B4-C65	A8-B4-C66
	A8-B4-C67	A8-B4-C68	A8-B4-C69	A8-B4-C70	A8-B4-C71	A8-B4-C72
30	A8-B4-C73	A8-B4-C74	A8-B4-C75	A8-B4-C76	A8-B4-C77	A8-B4-C78
	A8-B4-C79	A8-B4-C80	A8-B4-C81	A8-B4-C82	A8-B4-C83	A8-B4-C84
	A8-B4-C85	A8-B4-C86	A8-B4-C87	A8-B4-C88	A8-B4-C89	A8-B4-C90
	A8-B4-C91	A8-B4-C92	A8-B4-C93	A8-B4-C94	A8-B4-C95	A8-B4-C96
	A8-B4-C97	A8-B4-C98	A8-B4-C99	A8-B4-C100	A8-B4-C101	A8-B4-C102
35	A8-B4-C103	A8-B4-C104	A8-B4-C105	A8-B4-C106	A8-B4-C107	A8-B4-C108
	A8-B4-C109	A8-B4-C110	A8-B4-C111	A8-B4-C112	A8-B4-C113	A8-B4-C114
	A8-B4-C115	A8-B4-C116	A8-B4-C117	A8-B4-C118	A8-B4-C119	A8-B4-C120

	A8-B4-C121	A8-B4-C122	A8-B4-C123	A8-B4-C124	A8-B4-C125	A8-B4-C126
	A8-B4-C127	A8-B4-C128	A8-B4-C129	A8-B4-C130	A8-B4-C131	A8-B4-C132
	A8-B4-C133	A8-B4-C134	A8-B4-C135	A8-B4-C136	A8-B4-C137	A8-B4-C138
	A8-B4-C139	A8-B4-C140	BLANK	BLANK	BLANK	BLANK
5	A8-B5-C1	A8-B5-C2	A8-B5-C3	A8-B5-C4	A8-B5-C5	A8-B5-C6
	A8-B5-C7	A8-B5-C8	A8-B5-C9	A8-B5-C10	A8-B5-C11	A8-B5-C12
	A8-B5-C13	A8-B5-C14	A8-B5-C15	A8-B5-C16	A8-B5-C17	A8-B5-C18
	A8-B5-C19	A8-B5-C20	A8-B5-C21	A8-B5-C22	A8-B5-C23	A8-B5-C24
	A8-B5-C25	A8-B5-C26	A8-B5-C27	A8-B5-C28	A8-B5-C29	A8-B5-C30
10	A8-B5-C31	A8-B5-C32	A8-B5-C33	A8-B5-C34	A8-B5-C35	A8-B5-C36
-	A8-B5-C37	A8-B5-C38	A8-B5-C39	A8-B5-C40	A8-B5-C41	A8-B5-C42
	A8-B5-C43	A8-B5-C44	A8-B5-C45	A8-B5-C46	A8-B5-C47	A8-B5-C48
	A8-B5-C49	A8-B5-C50	A8-B5-C51	A8-B5-C52	A8-B5-C53	A8-B5-C54
	A8-B5-C55	A8-B5-C56	A8-B5-C57	A8-B5-C58	A8-B5-C59	A8-B5-C60
15	A8-B5-C61	A8-B5-C62	A8-B5-C63	A8-B5-C64	A8-B5-C65	A8-B5-C66
	A8-B5-C67	A8-B5-C68	A8-B5-C69	A8-B5-C70	A8-B5-C71	A8-B5-C72
	A8-B5-C73	A8-B5-C74	A8-B5-C75	A8-B5-C76	A8-B5-C77	A8-B5-C78
	A8-B5-C79	A8-B5-C80	A8-B5-C81	A8-B5-C82	A8-B5-C83	A8-B5-C84
	A8-B5-C85	A8-B5-C86	A8-B5-C87	A8-B5-C88	A8-B5-C89	A8-B5-C90
20	A8-B5-C91	A8-B5-C92	A8-B5-C93	A8-B5-C94	A8-B5-C95	A8-B5-C96
	A8-B5-C97	A8-B5-C98	A8-B5-C99	A8-B5-C100	A8-B5-C101	A8-B5-C102
	A8-B5-C103	A8-B5-C104	A8-B5-C105	A8-B5-C106	A8-B5-C107	A8-B5-C108
	A8-B5-C109	A8-B5-C110	A8-B5-C111	A8-B5-C112	A8-B5-C113	A8-B5-C114
	A8-B5-C115	A8-B5-C116	A8-B5-C117	A8-B5-C118	A8-B5-C119	A8-B5-C120
25	A8-B5-C121	A8-B5-C122	A8-B5-C123	A8-B5-C124	A8-B5-C125	A8-B5-C126
	A8-B5-C127	A8-B5-C128	A8-B5-C129	A8-B5-C130	A8-B5-C131	A8-B5-C132
	A8-B5-C133	A8-B5-C134	A8-B5-C135	A8-B5-C136	A8-B5-C137	A8-B5-C138
	A8-B5-C139	A8-B5-C140	BLANK	BLANK	BLANK	BLANK
	A8-B6-C1	A8-B6-C2	A8-B6-C3	A8-B6-C4	A8-B6-C5	A8-B6-C6
30	A8-B6-C7	A8-B6-C8	A8-B6-C9	A8-B6-C10	A8-B6-C11	A8-B6-C12
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	A8-B6-C19	A8-B6-C20	A8-B6-C21	A8-B6-C22	A8-B6-C23	A8-B6-C24
	A8-B6-C25	A8-B6-C26	A8-B6-C27	A8-B6-C28	A8-B6-C29	A8-B6-C30
	A8-B6-C31	A8-B6-C32	A8-B6-C33	A8-B6-C34	A8-B6-C35	A8-B6-C36
35	A8-B6-C37	A8-B6-C38	A8-B6-C39	A8-B6-C40	A8-B6-C41	A8-B6-C42
	A8-B6-C43	A8-B6-C44	A8-B6-C45	A8-B6-C46	A8-B6-C47	A8-B6-C48
	A8-B6-C49	A8-B6-C50	A8-B6-C51	A8-B6-C52	A8-B6-C53	A8-B6-C54

	A8-B6-C55	A8-B6-C56	A8-B6-C57	A8-B6-C58	A8-B6-C59	A8-B6-C60
	A8-B6-C61	A8-B6-C62	A8-B6-C63	A8-B6-C64	A8-B6-C65	A8-B6-C66
	A8-B6-C67	A8-B6-C68	A8-B6-C69	A8-B6-C70	A8-B6-C71	A8-B6-C72
	A8-B6-C73	A8-B6-C74	A8-B6-C75	A8-B6-C76	A8-B6-C77	A8-B6-C78
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	A8-B6-C85	A8-B6-C86	A8-B6-C87	A8-B6-C88	A8-B6-C89	A8-B6-C90
	A8-B6-C91	A8-B6-C92	A8-B6-C93	A8-B6-C94	A8-B6-C95	A8-B6-C96
	A8-B6-C97	A8-B6-C98	A8-B6-C99	A8-B6-C100	A8-B6-C101	A8-B6-C102
	A8-B6-C103	A8-B6-C104	A8-B6-C105	A8-B6-C106	A8-B6-C107	A8-B6-C108
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	A8-B6-C115	A8-B6-C116	A8-B6-C117	A8-B6-C118	A8-B6-C119	A8-B6-C120
	A8-B6-C121	A8-B6-C122	A8-B6-C123	A8-B6-C124	A8-B6-C125	A8-B6-C126
	A8-B6-C127	A8-B6-C128	A8-B6-C129	A8-B6-C130	A8-B6-C131	A8-B6-C132
	A8-B6-C133	A8-B6-C134	A8-B6-C135	A8-B6-C136	A8-B6-C137	A8-B6-C138
15	A8-B6-C139	A8-B6-C140	BLANK	BLANK	BLANK	BLANK
	A8-B7-C1	A8-B7-C2	A8-B7-C3	A8-B7-C4	A8-B7-C5	A8-B7-C6
	A8-B7-C7	A8-B7-C8	A8-B7-C9	A8-B7-C10	A8-B7-C11	A8-B7-C12
	A8-B7-C13	A8-B7-C14	A8-B7-C15	A8-B7-C16	A8-B7-C17	A8-B7-C18
	A8-B7-C19	A8-B7-C20	A8-B7-C21	A8-B7-C22	A8-B7-C23	A8-B7-C24
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	A8-B7-C43	A8-B7-C44	A8-B7-C45	A8-B7-C46	A8-B7-C47	A8-B7-C48
	A8-B7-C49	A8-B7-C50	A8-B7-C51	A8-B7-C52	A8-B7-C53	A8-B7-C54
25	A8-B7-C55	A8-B7-C56	A8-B7-C57	A8-B7-C58	A8-B7-C59	A8-B7-C60
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	A8-B7-C73	A8-B7-C74	A8-B7-C75	A8-B7-C76	A8-B7-C77	A8-B7-C78
	A8-B7-C79	A8-B7-C80	A8-B7-C81	A8-B7-C82	A8-B7-C83	A8-B7-C84
30	A8-B7-C85	A8-B7-C86	A8-B7-C87	A8-B7-C88	A8-B7-C89	A8-B7-C90
	A8-B7-C91	A8-B7-C92	A8-B7-C93	A8-B7-C94	A8-B7-C95	A8-B7-C96
	A8-B7-C97	A8-B7-C98	A8-B7-C99	A8-B7-C100	A8-B7-C101	A8-B7-C102
	A8-B7-C103	A8-B7-C104	A8-B7-C105	A8-B7-C106	A8-B7-C107	A8-B7-C108
	A8-B7-C109	A8-B7-C110	A8-B7-C111	A8-B7-C112	A8-B7-C113	A8-B7-C114
35	A8-B7-C115	A8-B7-C116	A8-B7-C117	A8-B7-C118	A8-B7-C119	A8-B7-C120
	A8-B7-C121	A8-B7-C122	A8-B7-C123	A8-B7-C124	A8-B7-C125	A8-B7-C126
	A8-B7-C127	A8-B7-C128	A8-B7-C129	A8-B7-C130	A8-B7-C131	A8-B7-C132

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	A8-B7-C133	A8-B7-C134	A8-B7-C135	A8-B7-C136	A8-B7-C137	A8-B7-C138
	A8-B7-C139	A8-B7-C140	BLANK	BLANK	BLANK	BLANK
	A8-B8-C1	A8-B8-C2	A8-B8-C3	A8-B8-C4	A8-B8-C5	A8-B8-C6
	A8-B8-C7	A8-B8-C8	A8-B8-C9	A8-B8-C10	A8-B8-C11	A8-B8-C12
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	A8-B8-C25	A8-B8-C26	A8-B8-C27	A8-B8-C28	A8-B8-C29	A8-B8-C30
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	A8-B8-C49	A8-B8-C50	A8-B8-C51	A8-B8-C52	A8-B8-C53	A8-B8-C54
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	A8-B8-C61	A8-B8-C62	A8-B8-C63	A8-B8-C64	A8-B8-C65	A8-B8-C66
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	A8-B8-C79	A8-B8-C80	A8-B8-C81	A8-B8-C82	A8-B8-C83	A8-B8-C84
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	A8-B8-C91	A8-B8-C92	A8-B8-C93	A8-B8-C94	A8-B8-C95	A8-B8-C96
	A8-B8-C97	A8-B8-C98	A8-B8-C99	A8-B8-C100	A8-B8-C101	A8-B8-C102
20	A8-B8-C103	A8-B8-C104	A8-B8-C105	A8-B8-C106	A8-B8-C107	A8-B8-C108
	A8-B8-C109	A8-B8-C110	A8-B8-C111	A8-B8-C112	A8-B8-C113	A8-B8-C114
	A8-B8-C115	A8-B8-C116	A8-B8-C117	A8-B8-C118	A8-B8-C119	A8-B8-C120
	A8-B8-C121	A8-B8-C122	A8-B8-C123	A8-B8-C124	A8-B8-C125	A8-B8-C126
	A8-B8-C127	A8-B8-C128	A8-B8-C129	A8-B8-C130	A8-B8-C131	A8-B8-C132
25	A8-B8-C133	A8-B8-C134	A8-B8-C135	A8-B8-C136	A8-B8-C137	A8-B8-C138
	A8-B8-C139	A8-B8-C140	BLANK	BLANK	BLANK	BLANK
	A8-B9-C1	A8-B9-C2	A8-B9-C3	A8-B9-C4	A8-B9-C5	A8-B9-C6
	A8-B9-C7	A8-B9-C8	A8-B9-C9	A8-B9-C10	A8-B9-C11	A8-B9-C12
	A8-B9-C13	A8-B9-C14	A8-B9-C15	A8-B9-C16	A8-B9-C17	A8-B9-C18
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	A8-B9-C25	A8-B9-C26	A8-B9-C27	A8-B9-C28	A8-B9-C29	A8-B9-C30
	A8-B9-C31	A8-B9-C32	A8-B9-C33	A8-B9-C34	A8-B9-C35	A8-B9-C36
	A8-B9-C37	A8-B9-C38	A8-B9-C39	A8-B9-C40	A8-B9-C41	A8-B9-C42
	A8-B9-C43	A8-B9-C44	A8-B9-C45	A8-B9-C46	A8-B9-C47	A8-B9-C48
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	A8-B9-C55	A8-B9-C56	A8-B9-C57	A8-B9-C58	A8-B9-C59	A8-B9-C60
	A8-B9-C61	A8-B9-C62	A8-B9-C63	A8-B9-C64	A8-B9-C65	A8-B9-C66

	A8-B9-C67	A8-B9-C68	A8-B9-C69	A8-B9-C70	A8-B9-C71	A8-B9-C72
	A8-B9-C73	A8-B9-C74	A8-B9-C75	A8-B9-C76	A8-B9-C77	A8-B9-C78
	A8-B9-C79	A8-B9-C80	A8-B9-C81	A8-B9-C82	A8-B9-C83	A8-B9-C84
	A8-B9-C85	A8-B9-C86	A8-B9-C87	A8-B9-C88	A8-B9-C89	A8-B9-C90
5	A8-B9-C91	A8-B9-C92	A8-B9-C93	A8-B9-C94	A8-B9-C95	A8-B9-C96
	A8-B9-C97	A8-B9-C98	A8-B9-C99	A8-B9-C100	A8-B9-C101	A8-B9-C102
	A8-B9-C103	A8-B9-C104	A8-B9-C105	A8-B9-C106	A8-B9-C107	A8-B9-C108
	A8-B9-C109	A8-B9-C110	A8-B9-C111	A8-B9-C112	A8-B9-C113	A8-B9-C114
	A8-B9-C115	A8-B9-C116	A8-B9-C117	A8-B9-C118	A8-B9-C119	A8-B9-C120
10	A8-B9-C121	A8-B9-C122	A8-B9-C123	A8-B9-C124	A8-B9-C125	A8-B9-C126
	A8-B9-C127	A8-B9-C128	A8-B9-C129	A8-B9-C130	A8-B9-C131	A8-B9-C132
	A8-B9-C133	A8-B9-C134	A8-B9-C135	A8-B9-C136	A8-B9-C137	A8-B9-C138
	A8-B9-C139	A8-B9-C140	BLANK	BLANK	BLANK	BLANK
	A8-B10-C1	A8-B10-C2	A8-B10-C3	A8-B10-C4	A8-B10-C5	A8-B10-C6
15	A8-B10-C7	A8-B10-C8	A8-B10-C9	A8-B10-C10	A8-B10-C11	A8-B10-C12
	A8-B10-C13	A8-B10-C14	A8-B10-C15	A8-B10-C16	A8-B10-C17	A8-B10-C18
	A8-B10-C19	A8-B10-C20	A8-B10-C21	A8-B10-C22	A8-B10-C23	A8-B10-C24
	A8-B10-C25	A8-B10-C26	A8-B10-C27	A8-B10-C28	A8-B10-C29	A8-B10-C30
•	A8-B10-C31	A8-B10-C32	A8-B10-C33	A8-B10-C34	A8-B10-C35	A8-B10-C36
20	A8-B10-C37	A8-B10-C38	A8-B10-C39	A8-B10-C40	A8-B10-C41	A8-B10-C42
	A8-B10-C43	A8-B10-C44	A8-B10-C45	A8-B10-C46	A8-B10-C47	A8-B10-C48
	A8-B10-C49	A8-B10-C50	A8-B10-C51	A8-B10-C52	A8-B10-C53	A8-B10-C54
	A8-B10-C55	A8-B10-C56	A8-B10-C57	A8-B10-C58	A8-B10-C59	A8-B10-C60
	A8-B10-C61	A8-B10-C62	A8-B10-C63	A8-B10-C64	A8-B10-C65	A8-B10-C66
25	A8-B10-C67	A8-B10-C68	A8-B10-C69	A8-B10-C70	A8-B10-C71	A8-B10-C72
	A8-B10-C73	A8-B10-C74	A8-B10-C75	A8-B10-C76	A8-B10-C77	A8-B10-C78
	A8-B10-C79	A8-B10-C80	A8-B10-C81	A8-B10-C82	A8-B10-C83	A8-B10-C84
	A8-B10-C85	A8-B10-C86	A8-B10-C87	A8-B10-C88	A8-B10-C89	A8-B10-C90
	A8-B10-C91	A8-B10-C92	A8-B10-C93	A8-B10-C94	A8-B10-C95	A8-B10-C96
30	A8-B10-C97	A8-B10-C98	A8-B10-C99	A8-B10-C100	A8-B10-C101	A8-B10-C102
	A8-B10-C103	A8-B10-C104	A8-B10-C105	A8-B10-C106	A8-B10-C107	A8-B10-C108
	A8-B10-C109	A8-B10-C110	A8-B10-C111	A8-B10-C112	A8-B10-C113	A8-B10-C114
	A8-B10-C115	A8-B10-C116	A8-B10-C117	A8-B10-C118	A8-B10-C119	A8-B10-C120
	A8-B10-C121	A8-B10-C122	A8-B10-C123	A8-B10-C124	A8-B10-C125	A8-B10-C126
35	A8-B10-C127	A8-B10-C128	A8-B10-C129	A8-B10-C130	A8-B10-C131	A8-B10-C132
	A8-B10-C133	A8-B10-C134	A8-B10-C135	A8-B10-C136	A8-B10-C137	A8-B10-C138
	A8-B10-C139	A8-B10-C140	BLANK	BLANK	BLANK	BLANK

	A8-B11-C1	A8-B11-C2	A8-B11-C3	A8-B11-C4	A8-B11-C5	A8-B11-C6
	A8-B11-C7	A8-B11-C8	A8-B11-C9	A8-B11-C10	A8-B11-C11	A8-B11-C12
	A8-B11-C13	A8-B11-C14	A8-B11-C15	A8-B11-C16	A8-B11-C17	A8-B11-C18
	A8-B11-C19	A8-B11-C20	A8-B11-C21	A8-B11-C22	A8-B11-C23	A8-B11-C24
5	A8-B11-C25	A8-B11-C26	A8-B11-C27	A8-B11-C28	A8-B11-C29	A8-B11-C30
	A8-B11-C31	A8-B11-C32	A8-B11-C33	A8-B11-C34	A8-B11-C35	A8-B11-C36
	A8-B11-C37	A8-B11-C38	A8-B11-C39	A8-B11-C40	A8-B11-C41	A8-B11-C42
	A8-B11-C43	A8-B11-C44	A8-B11-C45	A8-B11-C46	A8-B11-C47	A8-B11-C48
	A8-B11-C49	A8-B11-C50	A8-B11-C51	A8-B11-C52	A8-B11-C53	A8-B11-C54
10	A8-B11-C55	A8-B11-C56	A8-B11-C57	A8-B11-C58	A8-B11-C59	A8-B11-C60
	A8-B11-C61	A8-B11-C62	A8-B11-C63	A8-B11-C64	A8-B11-C65	A8-B11-C66
	A8-B11-C67	A8-B11-C68	A8-B11-C69	A8-B11-C70	A8-B11-C71	A8-B11-C72
	A8-B11-C73	A8-B11-C74	A8-B11-C75	A8-B11-C76	A8-B11-C77	A8-B11-C78
	A8-B11-C79	A8-B11-C80	A8-B11-C81	A8-B11-C82	A8-B11-C83	A8-B11-C84
15	A8-B11-C85	A8-B11-C86	A8-B11-C87	A8-B11-C88	A8-B11-C89	A8-B11-C90
	A8-B11-C91	A8-B11-C92	A8-B11-C93	A8-B11-C94	A8-B11-C95	A8-B11-C96
	A8-B11-C97	A8-B11-C98	A8-B11-C99	A8-B11-C100	A8-B11-C101	A8-B11-C102
	A8-B11-C103	A8-B11-C104	A8-B11-C105	A8-B11-C106	A8-B11-C107	A8-B11-C108
	A8-B11-C109	A8-B11-C110	A8-B1'1-C111	A8-B11-C112	A8-B11-C113	A8-B11-C114
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	A8-B11-C121	A8-B11-C122	A8-B11-C123	A8-B11-C124	A8-B11-C125	A8-B11-C126
	A8-B11-C127	A8-B11-C128	A8-B11-C129	A8-B11-C130	A8-B11-C131	A8-B11-C132
	A8-B11-C133	A8-B11-C134	A8-B11-C135	A8-B11-C136	A8-B11-C137	A8-B11-C138
	A8-B11-C139	A8-B11-C140	BLANK	BLANK	BLANK	BLANK
25	A8-B12-C1	A8-B12-C2	A8-B12-C3	A8-B12-C4	A8-B12-C5	A8-B12-C6
	A8-B12-C7	A8-B12-C8	A8-B12-C9	A8-B12-C10	A8-B12-C11	A8-B12-C12
	A8-B12-C13	A8-B12-C14	A8-B12-C15	A8-B12-C16	A8-B12-C17	A8-B12-C18
	A8-B12-C19	A8-B12-C20	A8-B12-C21	A8-B12-C22	A8-B12-C23	A8-B12-C24
	A8-B12-C25	A8-B12-C26	A8-B12-C27	A8-B12-C28	A8-B12-C29	A8-B12-C30
30	A8-B12-C31	A8-B12-C32	A8-B12-C33	A8-B12-C34	A8-B12-C35	A8-B12-C36
	A8-B12-C37	A8-B12-C38	A8-B12-C39	A8-B12-C40	A8-B12-C41	A8-B12-C42
	A8-B12-C43	A8-B12-C44	A8-B12-C45	A8-B12-C46	A8-B12-C47	A8-B12-C48
	A8-B12-C49	A8-B12-C50	A8-B12-C51	A8-B12-C52	A8-B12-C53	A8-B12-C54
	A8-B12-C55	A8-B12-C56	A8-B12-C57	A8-B12-C58	A8-B12-C59	A8-B12-C60
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	A8-B12-C67	A8-B12-C68	A8-B12-C69	A8-B12-C70	A8-B12-C71	A8-B12-C72
	A8-B12-C73	A8-B12-C74	A8-B12-C75	A8-B12-C76	A8-B12-C77	A8-B12-C78

	A8-B12-C79	A8-B12-C80	A8-B12-C81	A8-B12-C82	A8-B12-C83	A8-B12-C84
	A8-B12-C85	A8-B12-C86	A8-B12-C87	A8-B12-C88	A8-B12-C89	A8-B12-C90
	A8-B12-C91	A8-B12-C92	A8-B12-C93	A8-B12-C94	A8-B12-C95	A8-B12-C96
	A8-B12-C97	A8-B12-C98	A8-B12-C99	A8-B12-C100	A8-B12-C101	A8-B12-C102
5	A8-B12-C103	A8-B12-C104	A8-B12-C105	A8-B12-C106	A8-B12-C107	A8-B12-C108
	A8-B12-C109	A8-B12-C110	A8-B12-C111	A8-B12-C112	A8-B12-C113	A8-B12-C114
	A8-B12-C115	A8-B12-C116	A8-B12-C117	A8-B12-C118	A8-B12-C119	A8-B12-C120
	A8-B12-C121	A8-B12-C122	A8-B12-C123	A8-B12-C124	A8-B12-C125	A8-B12-C126
	A8-B12-C127	A8-B12-C128	A8-B12-C129	A8-B12-C130	A8-B12-C131	A8-B12-C132
10	A8-B12-C133	A8-B12-C134	A8-B12-C135	A8-B12-C136	A8-B12-C137	A8-B12-C138
	A8-B12-C139	A8-B12-C140	BLANK	BLANK	BLANK	BLANK
	A8-B13-C1	A8-B13-C2	A8-B13-C3	A8-B13-C4	A8-B13-C5	A8-B13-C6
	A8-B13-C7	A8-B13-C8	A8-B13-C9	A8-B13-C10	A8-B13-C11	A8-B13-C12
	A8-B13-C13	A8-B13-C14	A8-B13-C15	A8-B13-C16	A8-B13-C17	A8-B13-C18
15	A8-B13-C19	A8-B13-C20	A8-B13-C21	A8-B13-C22	A8-B13-C23	A8-B13-C24
	A8-B13-C25	A8-B13-C26	A8-B13-C27	A8-B13-C28	A8-B13-C29	A8-B13-C30
	A8-B13-C31	A8-B13-C32	A8-B13-C33	A8-B13-C34	A8-B13-C35	A8-B13-C36
	A8-B13-C37	A8-B13-C38	A8-B13-C39	A8-B13-C40	A8-B13-C41	A8-B13-C42
	A8-B13-C43	A8-B13-C44	A8-B13-C45	A8-B13-C46	A8-B13-C47	A8-B13-C48
20	A8-B13-C49	A8-B13-C50	A8-B13-C51	A8-B13-C52	A8-B13-C53	A8-B13-C54
	A8-B13-C55	A8-B13-C56	A8-B13-C57	A8-B13-C58	A8-B13-C59	A8-B13-C60
	A8-B13-C61	A8-B13-C62	A8-B13-C63	A8-B13-C64	A8-B13-C65	A8-B13-C66
	A8-B13-C67	A8-B13-C68	A8-B13-C69	A8-B13-C70	A8-B13-C71	A8-B13-C72
	A8-B13-C73	A8-B13-C74	A8-B13-C75	A8-B13-C76	A8-B13-C77	A8-B13-C78
25	A8-B13-C79	A8-B13-C80	A8-B13-C81	A8-B13-C82	A8-B13-C83	A8-B13-C84
	A8-B13-C85	A8-B13-C86	A8-B13-C87	A8-B13-C88	A8-B13-C89	A8-B13-C90
	A8-B13-C91	A8-B13-C92	A8-B13-C93	A8-B13-C94	A8-B13-C95	A8-B13-C96
	A8-B13-C97	A8-B13-C98	A8-B13-C99	A8-B13-C100	A8-B13-C101	A8-B13-C102
	A8-B13-C103	A8-B13-C104	A8-B13-C105	A8-B13-C106	A8-B13-C107	A8-B13-C108
30	A8-B13-C109	A8-B13-C110	A8-B13-C111	A8-B13-C112	A8-B13-C113	A8-B13-C114
	A8-B13-C115	A8-B13-C116	A8-B13-C117	A8-B13-C118	A8-B13-C119	A8-B13-C120
•	A8-B13-C121	A8-B13-C122	A8-B13-C123	A8-B13-C124	A8-B13-C125	A8-B13-C126
	A8-B13-C127	A8-B13-C128	A8-B13-C129	A8-B13-C130	A8-B13-C131	A8-B13-C132
	A8-B13-C133	A8-B13-C134	A8-B13-C135	A8-B13-C136	A8-B13-C137	A8-B13-C138
35	A8-B13-C139	A8-B13-C140	BLANK	BLANK	BLANK	BLANK
	A9-B1-C1	A9-B1-C2	A9-B1-C3	A9-B1-C4	A9-B1-C5	A9-B1-C6
	A9-B1-C7	A9-B1-C8	A9-B1-C9	A9-B1-C10	A9-B1-C11	A9-B1-C12

	A9-B1-C13	A9-B1-C14	A9-B1-C15	A9-B1-C16	A9-B1-C17	A9-B1-C18
	A9-B1-C19	A9-B1-C20	A9-B1-C21	A9-B1-C22	A9-B1-C23	A9-B1-C24
	A9-B1-C25	A9-B1-C26	. A9-B1-C27	A9-B1-C28	A9-B1-C29	A9-B1-C30
	A9-B1-C31	A9-B1-C32	A9-B1-C33	A9-B1-C34	A9-B1-C35	A9-B1-C36
5	A9-B1-C37	A9-B1-C38	A9-B1-C39	A9-B1-C40	A9-B1-C41	A9-B1-C42
	A9-B1-C43	A9-B1-C44	A9-B1-C45	A9-B1-C46	A9-B1-C47	A9-B1-C48
	A9-B1-C49	A9-B1-C50	A9-B1-C51	A9-B1-C52	A9-B1-C53	A9-B1-C54
	A9-B1-C55	A9-B1-C56	A9-B1-C57	A9-B1-C58	A9-B1-C59	A9-B1-C60
	A9-B1-C61	A9-B1-C62	A9-B1-C63	A9-B1-C64	A9-B1-C65	A9-B1-C66
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	A9-B1-C73	A9-B1-C74	A9-B1-C75	A9-B1-C76	A9-B1-C77	A9-B1-C78
	A9-B1-C79	A9-B1-C80	A9-B1-C81	A9-B1-C82	A9-B1-C83	A9-B1-C84
	A9-B1-C85	A9-B1-C86	A9-B1-C87	A9-B1-C88	A9-B1-C89	A9-B1-C90
	A9-B1-C91	A9-B1-C92	A9-B1-C93	A9-B1-C94	A9-B1-C95	A9-B1-C96
15	A9-B1-C97	A9-B1-C98	A9-B1-C99	A9-B1-C100	A9-B1-C101	A9-B1-C102
	A9-B1-C103	A9-B1-C104	A9-B1-C105	A9-B1-C106	A9-B1-C107	A9-B1-C108
	A9-B1-C109	A9-B1-C110	A9-B1-C111	A9-B1-C112	A9-B1-C113	A9-B1-C114
	A9-B1-C115	A9-B1-C116	A9-B1-C117	A9-B1-C118	A9-B1-C119	A9-B1-C120
	A9-B1-C121	A9-B1-C122	A9-B1-C123	A9-B1-C124	A9-B1-C125	A9-B1-C126
20	A9-B1-C127	A9-B1-C128	A9-B1-C129	A9-B1-C130	A9-B1-C131	A9-B1-C132
	A9-B1-C133	A9-B1-C134	A9-B1-C135	A9-B1-C136	A9-B1-C137	A9-B1-C138
	A9-B1-C139	A9-B1-C140	BLANK	BLANK	BLANK	BLANK
	A9-B2-C1	A9-B2-C2	A9-B2-C3	A9-B2-C4	A9-B2-C5	A9-B2-C6
	A9-B2-C7	A9-B2-C8	A9-B2-C9	A9-B2-C10	A9-B2-C11	A9-B2-C12
25	A9-B2-C13	A9-B2-C14	A9-B2-C15	A9-B2-C16	A9-B2-C17	A9-B2-C18
	A9-B2-C19	A9-B2-C20	A9-B2-C21	A9-B2-C22	A9-B2-C23	A9-B2-C24
	A9-B2-C25	A9-B2-C26	A9-B2-C27	A9-B2-C28	A9-B2-C29	A9-B2-C30
	A9-B2-C31	A9-B2-C32	A9-B2-C33	A9-B2-C34	A9-B2-C35	A9-B2-C36
	A9-B2-C37	A9-B2-C38	A9-B2-C39	A9-B2-C40	A9-B2-C41	A9-B2-C42
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	A9-B2-C61	A9-B2-C62	A9-B2-C63	A9-B2-C64	A9-B2-C65	A9-B2-C66
	A9-B2-C67	A9-B2-C68	A9-B2-C69	A9-B2-C70	A9-B2-C71	A9-B2-C72
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	A9-B2-C79	A9-B2-C80	A9-B2-C81	A9-B2-C82	A9-B2-C83	A9-B2-C84
	A9-B2-C85	A9-B2-C86	A9-B2-C87	A9-B2-C88	A9-B2-C89	A9-B2-C90

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	A9-B2-C97	A9-B2-C98	A9-B2-C99	A9-B2-C100	A9-B2-C101	A9-B2-C102
	A9-B2-C103	A9-B2-C104	A9-B2-C105	A9-B2-C106	A9-B2-C107	A9-B2-C108
	A9-B2-C109	A9-B2-C110	A9-B2-C111	A9-B2-C112	A9-B2-C113	A9-B2-C114
5	A9-B2-C115	A9-B2-C116	A9-B2-C117	A9-B2-C118	A9-B2-C119	A9-B2-C120
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	A9-B2-C127	A9-B2-C128	A9-B2-C129	A9-B2-C130	A9-B2-C131	A9-B2-C132
	A9-B2-C133	A9-B2-C134	A9-B2-C135	A9-B2-C136	A9-B2-C137	A9-B2-C138
	A9-B2-C139	A9-B2-C140	BLANK	BLANK	BLANK	BLANK
10	A9-B3-C1	A9-B3-C2	A9-B3-C3	A9-B3-C4	A9-B3-C5	A9-B3-C6
	A9-B3-C7	A9-B3-C8	A9-B3-C9	A9-B3-C10	A9-B3-C11	A9-B3-C12
	A9-B3-C13	A9-B3-C14	A9-B3-C15	A9-B3-C16	A9-B3-C17	A9-B3-C18
	A9-B3-C19	A9-B3-C20	A9-B3-C21	A9-B3-C22	A9-B3-C23	A9-B3-C24
	A9-B3-C25	A9-B3-C26	A9-B3-C27	A9-B3-C28	A9-B3-C29	A9-B3-C30
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	A9-B3-C43	A9-B3-C44	A9-B3-C45	A9-B3-C46	A9-B3-C47	A9-B3-C48
	A9-B3-C49	A9-B3-C50	A9-B3-C51	A9-B3-C52	A9-B3-C53	A9-B3-C54
	A9-B3-C55	A9-B3-C56	A9-B3-C57	A9-B3-C58	A9-B3-C59	A9-B3-C60
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	A9-B3-C67	A9-B3-C68	A9-B3-C69	A9-B3-C70	A9-B3-C71	A9-B3-C72
	A9-B3-C73	A9-B3-C74	A9-B3-C75	A9-B3-C76	A9-B3-C77	A9-B3-C78
	A9-B3-C79	A9-B3-C80	A9-B3-C81	A9-B3-C82	A9-B3-C83	A9-B3-C84
	A9-B3-C85	A9-B3-C86	A9-B3-C87	A9-B3-C88	A9-B3-C89	A9-B3-C90
25	A9-B3-C91	A9-B3-C92	A9-B3-C93	A9-B3-C94	A9-B3-C95	A9-B3-C96
	A9-B3-C97	A9-B3-C98	A9-B3-C99	A9-B3-C100	A9-B3-C101	A9-B3-C102
	A9-B3-C103	A9-B3-C104	A9-B3-C105	A9-B3-C106	A9-B3-C107	A9-B3-C108
	A9-B3-C109	A9-B3-C110	A9-B3-C111	A9-B3-C112	A9-B3-C113	A9-B3-C114
	A9-B3-C115	A9-B3-C116	A9-B3-C117	A9-B3-C118	A9-B3-C119	A9-B3-C120
30	A9-B3-C121	A9-B3-C122	A9-B3-C123	A9-B3-C124	A9-B3-C125	A9-B3-C126
	A9-B3-C127	A9-B3-C128	A9-B3-C129	A9-B3-C130	A9-B3-C131	A9-B3-C132
	A9-B3-C133	A9-B3-C134	A9-B3-C135	A9-B3-C136	A9-B3-C137	A9-B3-C138
	A9-B3-C139	A9-B3-C140	BLANK	BLANK	BLANK	BLANK
	A9-B4-C1	A9-B4-C2	A9-B4-C3	A9-B4-C4	A9-B4-C5	A9-B4-C6
35	A9-B4-C7	A9-B4-C8	A9-B4-C9	A9-B4-C10	A9-B4-C11	A9-B4-C12
	A9-B4-C13	A9-B4-C14	A9-B4-C15	A9-B4-C16	A9-B4-C17	A9-B4-C18
	A9-B4-C19	A9-B4-C20	A9-B4-C21	A9-B4-C22	A9-B4-C23	A9-B4-C24

	A9-B4-C25	A9-B4-C26	A9-B4-C27	A9-B4-C28	A9-B4-C29	A9-B4-C30
	A9-B4-C31	A9-B4-C32	A9-B4-C33	A9-B4-C34	A9-B4-C35	A9-B4-C36
	A9-B4-C37	A9-B4-C38	A9-B4-C39	A9-B4-C40	A9-B4-C41	A9-B4-C42
	A9-B4-C43	A9-B4-C44	A9-B4-C45	A9-B4-C46	A9-B4-C47	A9-B4-C48
5	A9-B4-C49	A9-B4-C50	A9-B4-C51	A9-B4-C52	A9-B4-C53	A9-B4-C54
	A9-B4-C55	A9-B4-C56	A9-B4-C57	A9-B4-C58	A9-B4-C59	A9-B4-C60
	A9-B4-C61	A9-B4-C62	A9-B4-C63	A9-B4-C64	A9-B4-C65	A9-B4-C66
	A9-B4-C67	A9-B4-C68	A9-B4-C69	A9-B4-C70	A9-B4-C71	A9-B4-C72
	A9-B4-C73	A9-B4-C74	A9-B4-C75	A9-B4-C76	A9-B4-C77	A9-B4-C78
10	A9-B4-C79	A9-B4-C80	A9-B4-C81	A9-B4-C82	A9-B4-C83	A9-B4-C84
	A9-B4-C85	A9-B4-C86	A9-B4-C87	A9-B4-C88	A9-B4-C89	A9-B4-C90
	A9-B4-C91	A9-B4-C92	A9-B4-C93	A9-B4-C94	A9-B4-C95	A9-B4-C96
	A9-B4-C97	A9-B4-C98	A9-B4-C99	A9-B4-C100	A9-B4-C101	A9-B4-C102
	A9-B4-C103	A9-B4-C104	A9-B4-C105	A9-B4-C106	A9-B4-C107	A9-B4-C108
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	A9-B4-C115	A9-B4-C116	A9-B4-C117	A9-B4-C118	A9-B4-C119	A9-B4-C120
	A9-B4-C121	A9-B4-C122	A9-B4-C123	A9-B4-C124	A9-B4-C125	A9-B4-C126
	A9-B4-C127	A9-B4-C128	A9-B4-C129	A9-B4-C130	A9-B4-C131	A9-B4-C132
	A9-B4-C133	A9-B4-C134	A9-B4-C135	A9-B4-C136	A9-B4-C137	A9-B4-C138
20	A9-B4-C139	A9-B4-C140	BLANK	BLANK	BLANK	BLANK
	A9-B5-C1	A9-B5-C2	A9-B5-C3	A9-B5-C4	A9-B5-C5	A9-B5-C6
	A9-B5-C7	A9-B5-C8	A9-B5-C9	A9-B5-C10	A9-B5-C11	A9-B5-C12
	A9-B5-C13	A9-B5-C14	A9-B5-C15	A9-B5-C16	A9-B5-C17	A9-B5-C18
	A9-B5-C19	A9-B5-C20	A9-B5-C21	A9-B5-C22	A9-B5-C23	A9-B5-C24
25	A9-B5-C25	A9-B5-C26	A9-B5-C27	A9-B5-C28	A9-B5-C29	A9-B5-C30
	A9-B5-C31	A9-B5-C32	A9-B5-C33	A9-B5-C34	A9-B5-C35	A9-B5-C36
	A9-B5-C37	A9-B5-C38	A9-B5-C39	A9-B5-C40	A9-B5-C41	A9-B5-C42
	A9-B5-C43	A9-B5-C44	A9-B5-C45	A9-B5-C46	A9-B5-C47	A9-B5-C48
	A9-B5-C49	A9-B5-C50	A9-B5-C51	A9-B5-C52	A9-B5-C53	A9-B5-C54
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	A9-B5-C61	A9-B5-C62	A9-B5-C63	A9-B5-C64	A9-B5-C65	A9-B5-C66
	A9-B5-C67	A9-B5-C68	A9-B5-C69	A9-B5-C70	A9-B5-C71	A9-B5-C72
	A9-B5-C73	A9-B5-C74	A9-B5-C75	A9-B5-C76	A9-B5-C77	A9-B5-C78
	A9-B5-C79	A9-B5-C80	A9-B5-C81	A9-B5-C82	A9-B5-C83	A9-B5-C84
35	A9-B5-C85	A9-B5-C86	A9-B5-C87	A9-B5-C88	A9-B5-C89	A9-B5-C90
	A9-B5-C91	A9-B5-C92	A9-B5-C93	A9-B5-C94	A9-B5-C95	A9-B5-C96
	A9-B5-C97	A9-B5-C98	A9-B5-C99	A9-B5-C100	A9-B5-C101	A9-B5-C102

	A9-B5-C103	A9-B5-C104	A9-B5-C105	A9-B5-C106	A9-B5-C107	A9-B5-C108
	A9-B5-C109	A9-B5-C110	A9-B5-C111	A9-B5-C112	A9-B5-C113	A9-B5-C114
	A9-B5-C115	A9-B5-C116	A9-B5-C117	A9-B5-C118	A9-B5-C119	A9-B5-C120
	A9-B5-C121	A9-B5-C122	A9-B5-C123	A9-B5-C124	A9-B5-C125	A9-B5-C126
5	A9-B5-C127	A9-B5-C128	A9-B5-C129	A9-B5-C130	A9-B5-C131	A9-B5-C132
	A9-B5-C133	A9-B5-C134	A9-B5-C135	A9-B5-C136	A9-B5-C137	A9-B5-C138
	A9-B5-C139	A9-B5-C140	BLANK	BLANK	BLANK	BLANK
	A9-B6-C1	A9-B6-C2	A9-B6-C3	A9-B6-C4	A9-B6-C5	A9-B6-C6
	A9-B6-C7	A9-B6-C8	A9-B6-C9	A9-B6-C10	A9-B6-C11	A9-B6-C12
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	A9-B6-C19	A9-B6-C20	A9-B6-C21	A9-B6-C22	A9-B6-C23	A9-B6-C24
	A9-B6-C25	A9-B6-C26	A9-B6-C27	A9-B6-C28	A9-B6-C29	A9-B6-C30
	A9-B6-C31	A9-B6-C32	A9-B6-C33	A9-B6-C34	A9-B6-C35	A9-B6-C36
	A9-B6-C37	A9-B6-C38	A9-B6-C39	A9-B6-C40	A9-B6-C41	A9-B6-C42
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	A9-B6-C49	A9-B6-C50	A9-B6-C51	A9-B6-C52	A9-B6-C53	A9-B6-C54
	A9-B6-C55	A9-B6-C56	A9-B6-C57	A9-B6-C58	A9-B6-C59	A9-B6-C60
	A9-B6-C61	A9-B6-C62	A9-B6-C63	A9-B6-C64	A9-B6-C65	A9-B6-C66
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	A9-B6-C85	A9-B6-C86	A9-B6-C87	A9-B6-C88	A9-B6-C89	A9-B6-C90
	A9-B6-C91	A9-B6-C92	A9-B6-C93	A9-B6-C94	A9-B6-C95	A9-B6-C96
	A9-B6-C97	A9-B6-C98	A9-B6-C99	A9-B6-C100	A9-B6-C101	A9-B6-C102
25	A9-B6-C103	A9-B6-C104	A9-B6-C105	A9-B6-C106	A9-B6-C107	A9-B6-C108
	A9-B6-C109	A9-B6-C110	A9-B6-C111	A9-B6-C112	A9-B6-C113	A9-B6-C114
	A9-B6-C115	A9-B6-C116	A9-B6-C117	A9-B6-C118	A9-B6-C119	A9-B6-C120
	A9-B6-C121	A9-B6-C122	A9-B6-C123	A9-B6-C124	A9-B6-C125	A9-B6-C126
	A9-B6-C127	A9-B6-C128	A9-B6-C129	A9-B6-C130	A9-B6-C131	A9-B6-C132
30	A9-B6-C133	A9-B6-C134	A9-B6-C135	A9-B6-C136	A9-B6-C137	A9-B6-C138
	A9-B6-C139	A9-B6-C140	BLANK	BLANK	BLANK	BLANK
	A9-B7-C1	A9-B7-C2	A9-B7-C3	A9-B7-C4	A9-B7-C5	A9-B7-C6
	A9-B7-C7	A9-B7-C8	A9-B7-C9	A9-B7-C10	A9-B7-C11	A9-B7-C12
	A9-B7-C13	A9-B7-C14	A9-B7-C15	A9-B7-C16	A9-B7-C17	A9-B7-C18
35	A9-B7-C19	A9-B7-C20	A9-B7-C21	A9-B7-C22	A9-B7-C23	A9-B7-C24
	A9-B7-C25	A9-B7-C26	A9-B7-C27	A9-B7-C28	A9-B7-C29	A9-B7-C30
	A9-B7-C31	A9-B7-C32	A9-B7-C33	A9-B7-C34	A9-B7-C35	A9-B7-C36

	A9-B7-C37	A9-B7-C38	A9-B7-C39	A9-B7-C40	A9-B7-C41	A9-B7-C42
	A9-B7-C43	A9-B7-C44	A9-B7-C45	A9-B7-C46	A9-B7-C47	A9-B7-C48
	A9-B7-C49	A9-B7-C50	A9-B7-C51	A9-B7-C52	A9-B7-C53	A9-B7-C54
	A9-B7-C55	A9-B7-C56	A9-B7-C57	A9-B7-C58	A9-B7-C59	A9-B7-C60
5	A9-B7-C61	A9-B7-C62	A9-B7-C63	A9-B7-C64	A9-B7-C65	A9-B7-C66
	A9-B7-C67	A9-B7-C68	A9-B7-C69	A9-B7-C70	A9-B7-C71	A9-B7-C72
	A9-B7-C73	A9-B7-C74	A9-B7-C75	A9-B7-C76	A9-B7-C77	A9-B7-C78
	A9-B7 - C79	A9-B7-C80	A9-B7-C81	A9-B7-C82	A9-B7-C83	A9-B7-C84
	A9-B7-C85	A9-B7-C86	A9-B7-C87	A9-B7-C88	A9-B7-C89	A9-B7-C90
10	A9-B7-C91	A9-B7-C92	A9-B7-C93	A9-B7-C94	A9-B7-C95	A9-B7-C96
	A9-B7-C97	A9-B7-C98	A9-B7-C99	A9-B7-C100	A9-B7-C101	A9-B7-C102
	A9-B7-C103	A9-B7-C104	A9-B7-C105	A9-B7-C106	A9-B7-C107	A9-B7-C108
	A9-B7-C109	A9-B7-C110	A9-B7-C111	A9-B7-C112	A9-B7-C113	A9-B7-C114
	A9-B7-C115	A9-B7-C116	A9-B7-C117	A9-B7-C118	A9-B7-C119	A9-B7-C120
15	A9-B7-C121	A9-B7-C122	A9-B7-C123	A9-B7-C124	A9-B7-C125	A9-B7-C126
	A9-B7-C127	A9-B7-C128	A9-B7-C129	A9-B7-C130	A9-B7-C131	A9-B7-C132
	A9-B7-C133	A9-B7-C134	A9-B7-C135	A9-B7-C136	A9-B7-C137	A9-B7-C138
	A9-B7-C139	A9-B7-C140	BLANK	BLANK	BLANK	BLANK
	A9-B8-C1	A9-B8-C2	A9-B8-C3	A9-B8-C4	A9-B8-C5	A9-B8-C6
20	A9-B8-C7	A9-B8-C8	A9-B8-C9	A9-B8-C10	A9-B8-C11	A9-B8-C12
	A9-B8-C13	A9-B8-C14	A9-B8-C15	A9-B8-C16	A9-B8-C17	A9-B8-C18
	A9-B8-C19	A9-B8-C20	A9-B8-C21	A9-B8-C22	A9-B8-C23	A9-B8-C24
	A9-B8-C25	A9-B8-C26	A9-B8-C27	A9-B8-C28	A9-B8-C29	A9-B8-C30
	A9-B8-C31	A9-B8-C32	A9-B8-C33	A9-B8-C34	A9-B8-C35	A9-B8-C36
25	A9-B8-C37	A9-B8-C38	A9-B8-C39	A9-B8-C40	A9-B8-C41	A9-B8-C42
	A9-B8-C43	A9-B8-C44	A9-B8-C45	A9-B8-C46	A9-B8-C47	A9-B8-C48
	A9-B8-C49	A9-B8-C50	A9-B8-C51	A9-B8-C52	A9-B8-C53	A9-B8-C54
	A9-B8-C55	A9-B8-C56	A9-B8-C57	A9-B8-C58	A9-B8-C59	A9-B8-C60
	A9-B8-C61	A9-B8-C62	A9-B8-C63	A9-B8-C64	A9-B8-C65	A9-B8-C66
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	A9-B8-C73	A9-B8-C74	A9-B8-C75	A9-B8-C76	A9-B8-C77	A9-B8-C78
	A9-B8-C79	A9-B8-C80	A9-B8-C81	A9-B8-C82	A9-B8-C83	A9-B8-C84
	A9-B8-C85	A9-B8-C86	A9-B8-C87	A9-B8-C88	A9-B8-C89	A9-B8-C90
	A9-B8-C91	A9-B8-C92	A9-B8-C93	A9-B8-C94	A9-B8-C95	A9-B8-C96
35	A9-B8-C97	A9-B8-C98	A9-B8-C99	A9-B8-C100	A9-B8-C101	A9-B8-C102
	A9-B8-C103	A9-B8-C104	A9-B8-C105	A9-B8-C106	A9-B8-C107	A9-B8-C108
	A9-B8-C109	A9-B8-C110	A9-B8-C111	A9-B8-C112	A9-B8-C113	A9-B8-C114

	A9-B8-C115	A9-B8-C116	A9-B8-C117	A9-B8-C118	A9-B8-C119	A9-B8-C120
	A9-B8-C121	A9-B8-C122	A9-B8-C123	A9-B8-C124	A9-B8-C125	A9-B8-C126
	A9-B8-C127	A9-B8-C128	A9-B8-C129	A9-B8-C130	A9-B8-C131	A9-B8-C132
	A9-B8-C133	A9-B8-C134	A9-B8-C135	A9-B8-C136	A9-B8-C137	A9-B8-C138
5	A9-B8-C139	A9-B8-C140	BLANK	BLANK	BLANK	BLANK
	A9-B9-C1	A9-B9-C2	A9-B9-C3	A9-B9-C4	A9-B9-C5	A9-B9-C6
	A9-B9-C7	A9-B9-C8	A9-B9-C9	A9-B9-C10	A9-B9-C11	A9-B9-C12
	A9-B9-C13	A9-B9-C14	A9-B9-C15	A9-B9-C16	A9-B9-C17	A9-B9-C18
	A9-B9-C19	A9-B9-C20	A9-B9-C21	A9-B9-C22	A9-B9-C23	A9-B9-C24
10	A9-B9-C25	A9-B9-C26	A9-B9-C27	A9-B9-C28	A9-B9-C29	A9-B9-C30
	A9-B9-C31	A9-B9-C32	A9-B9-C33	A9-B9-C34	A9-B9-C35	A9-B9-C36
	A9-B9-C37	A9-B9-C38	A9-B9-C39	A9-B9-C40	A9-B9-C41	A9-B9-C42
	A9-B9-C43	A9-B9-C44	A9-B9-C45	A9-B9 - C46	A9-B9-C47	A9-B9-C48
	A9-B9-C49	A9-B9-C50	A9-B9-C51	A9-B9-C52	A9-B9-C53	A9-B9-C54
15	A9-B9-C55	A9-B9-C56	A9-B9-C57	A9-B9-C58	A9-B9-C59	A9-B9-C60
	A9-B9-C61	A9-B9-C62	A9-B9-C63	A9-B9-C64	A9-B9-C65	A9-B9-C66
	A9-B9-C67	A9-B9-C68	A9-B9-C69	A9-B9-C70	A9-B9-C71	A9-B9-C72
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	A9-B9-C103	A9-B9-C104	A9-B9-C105	A9-B9-C106	A9-B9-C107	A9-B9-C108
	A9-B9-C109	A9-B9-C110	A9-B9-C111	A9-B9-C112	A9-B9-C113	A9-B9-C114
25	A9-B9-C115	A9-B9-C116	A9-B9-C117	A9-B9-C118	A9-B9-C119	A9-B9-C120
	A9-B9-C121	A9-B9-C122	A9-B9-C123	A9-B9-C124	A9-B9-C125	A9-B9-C126
	A9-B9-C127	A9-B9-C128	A9-B9-C129	A9-B9-C130	A9-B9-C131	A9-B9-C132
	A9-B9-C133	A9-B9-C134	A9-B9-C135	A9-B9-C136	A9-B9-C137	A9-B9-C138
	A9-B9-C1 3 9	A9-B9-C140	BLANK	BLANK	BLANK	BLANK
30	A9-B10-C1	A9-B10-C2	A9-B10-C3	A9-B10-C4	A9-B10-C5	A9-B10-C6
	A9-B10-C7	A9-B10-C8	A9-B10-C9	A9-B10-C10	A9-B10-C11	A9-B10-C12
	A9-B10-C13	A9-B10-C14	A9-B10-C15	A9-B10-C16	A9-B10-C17	A9-B10-C18
	A9-B10-C19	A9-B10-C20	A9-B10-C21	A9-B10-C22	A9-B10-C23	A9-B10-C24
	A9-B10-C25	A9-B10-C26	A9-B10-C27	A9-B10-C28	A9-B10-C29	A9-B10-C30
35	A9-B10-C31	A9-B10-C32	A9-B10-C33	A9-B10-C34	A9-B10-C35	A9-B10-C36
	A9-B10-C37	A9-B10-C38	A9-B10-C39	A9-B10-C40	A9-B10-C41	A9-B10-C42
	A9-B10-C43	A9-B10-C44	A9-B10-C45	A9-B10-C46	A9-B10-C47	A9-B10-C48

	A9-B10-C49	A9-B10-C50	A9-B10-C51	A9-B10-C52	A9-B10-C53	A9-B10-C54
	A9-B10-C55	A9-B10-C56	A9-B10-C57	A9-B10-C58	A9-B10-C59	A9-B10-C60
	A9-B10-C61	A9-B10-C62	A9-B10-C63	A9-B10-C64	A9-B10-C65	A9-B10-C66
	A9-B10-C67	A9-B10-C68	A9-B10-C69	A9-B10-C70	A9-B10-C71	A9-B10-C72
5	A9-B10-C73	A9-B10-C74	A9-B10-C75	A9-B10-C76	A9-B10-C77	A9-B10-C78
	A9-B10-C79	A9-B10-C80	A9-B10-C81	A9-B10-C82	A9-B10-C83	A9-B10-C84
	A9-B10-C85	A9-B10-C86	A9-B10-C87	A9-B10-C88	A9-B10-C89	A9-B10-C90
	A9-B10-C91	A9-B10-C92	A9-B10-C93	A9-B10-C94	A9-B10-C95	A9-B10-C96
	A9-B10-C97	A9-B10-C98	A9-B10-C99	A9-B10-C100	A9-B10-C101	A9-B10-C102
10	A9-B10-C103	A9-B10-C104	A9-B10-C105	A9-B10-C106	A9-B10-C107	A9-B10-C108
-	A9-B10-C109	A9-B10-C110	A9-B10-C111	A9-B10-C112	A9-B10-C113	A9-B10-C114
	A9-B10-C115	A9-B10-C116	A9-B10-C117	A9-B10-C118	A9-B10-C119	A9-B10-C120
	A9-B10-C121	A9-B10-C122	A9-B10-C123	A9-B10-C124	A9-B10-C125	A9-B10-C126
	A9-B10-C127	A9-B10-C128	A9-B10-C129	A9-B10-C130	A9-B10-C131	A9-B10-C132
15	A9-B10-C133	A9-B10-C134	A9-B10-C135	A9-B10-C136	A9-B10-C137	A9-B10-C138
	A9-B10-C139	A9-B10-C140	BLANK	BLANK	BLANK	BLANK
	A9-B11-C1	A9-B11-C2	A9-B11-C3	A9-B11-C4	A9-B11-C5	A9-B11-C6
•	A9-B11-C7	A9-B11-C8	A9-B11-C9	A9-B11-C10	A9-B11-C11	A9-B11-C12
	A9-B11-C13	A9-B11-C14	A9-B11-C15	A9-B11-C16	A9-B11-C17	A9-B11-C18
20	A9-B11-C19	A9-B11-C20	A9-B11-C21	A9-B11-C22	A9-B11-C23	A9-B11-C24
	A9-B11-C25	A9-B11-C26	A9-B11-C27	A9-B11-C28	A9-B11-C29	A9-B11-C30
	A9-B11-C31	A9-B11-C32	A9-B11-C33	A9-B11-C34	A9-B11-C35	A9-B11-C36
	A9-B11-C37	A9-B11-C38	A9-B11-C39	A9-B11-C40	A9-B11-C41	A9-B11-C42
	A9-B11-C43	A9-B11-C44	A9-B11-C45	A9-B11-C46	A9-B11-C47	A9-B11-C48
25	A9-B11-C49	A9-B11-C50	A9-B11-C51	A9-B11-C52	A9-B11-C53	A9-B11-C54
	A9-B11-C55	A9-B11-C56	A9-B11-C57	A9-B11-C58	A9-B11-C59	A9-B11-C60
	A9-B11-C61	A9-B11-C62	A9-B11-C63	A9-B11-C64	A9-B11-C65	A9-B11-C66
	A9-B11-C67	A9-B11-C68	A9-B11-C69	A9-B11-C70	A9-B11-C71	A9-B11-C72
	A9-B11-C73	A9-B11-C74	A9-B11-C75	A9-B11-C76	A9-B11-C77	A9-B11-C78
30	A9-B11-C79	A9-B11-C80	A9-B11-C81	A9-B11-C82	A9-B11-C83	A9-B11-C84
	A9-B11-C85	A9-B11-C86	A9-B11-C87	A9-B11-C88	A9-B11-C89	A9-B11-C90
	A9-B11-C91	A9-B11-C92	A9-B11-C93	A9-B11-C94	A9-B11-C95	A9-B11-C96
	A9-B11-C97	A9-B11-C98	A9-B11-C99	A9-B11-C100	A9-B11-C101	A9-B11-C102
	A9-B11-C103	A9-B11-C104	A9-B11-C105	A9-B11-C106	A9-B11-C107	A9-B11-C108
35	A9-B11-C109	A9-B11-C110	A9-B11-C111	A9-B11-C112	A9-B11-C113	A9-B11-C114
	A9-B11-C115	A9-B11-C116	A9-B11-C117	A9-B11-C118	A9-B11-C119	A9-B11-C120
	A9-B11-C121	A9-B11-C122	A9-B11-C123	A9-B11-C124	A9-B11-C125	A9-B11-C126

	A9-B11-C127	A9-B11-C128	A9-B11-C129	A9-B11-C130	A9-B11-C131	A9-B11-C132
	A9-B11-C133	A9-B11-C134	A9-B11-C135	A9-B11-C136	A9-B11-C137	A9-B11-C138
	A9-B11-C139	A9-B11-C140	BLANK	BLANK	BLANK	BLANK
	A9-B12-C1	A9-B12-C2	A9-B12-C3	A9-B12-C4	A9-B12-C5	A9-B12-C6
5	A9-B12-C7	A9-B12-C8	A9-B12-C9	A9-B12-C10	A9-B12-C11	A9-B12-C12
	A9-B12-C13	A9-B12-C14	A9-B12-C15	A9-B12-C16	A9-B12-C17	A9-B12-C18
	A9-B12-C19	A9-B12-C20	A9-B12-C21	A9-B12-C22	A9-B12-C23	A9-B12-C24
	A9-B12-C25	A9-B12-C26	A9-B12-C27	A9-B12-C28	A9-B12-C29	A9-B12-C30
	A9-B12-C31	A9-B12-C32	A9-B12-C33	A9-B12-C34	A9-B12-C35	A9-B12-C36
10	A9-B12-C37	A9-B12-C38	A9-B12-C39	A9-B12-C40	A9-B12-C41	A9-B12-C42
	A9-B12-C43	A9-B12-C44	A9-B12-C45	A9-B12-C46	A9-B12-C47	A9-B12-C48
	A9-B12-C49	A9-B12-C50	A9-B12-C51	A9-B12-C52	A9-B12-C53	A9-B12-C54
	A9-B12-C55	A9-B12-C56	A9-B12-C57	A9-B12-C58	A9-B12-C59	A9-B12-C60
	A9-B12-C61	A9-B12-C62	A9-B12-C63	A9-B12-C64	A9-B12-C65	A9-B12-C66
15	A9-B12-C67	A9-B12-C68	A9-B12-C69	A9-B12-C70	A9-B12-C71	A9-B12-C72
	A9-B12-C73	A9-B12-C74	A9-B12-C75	A9-B12-C76	A9-B12-C77	A9-B12-C78
	A9-B12-C79	A9-B12-C80	A9-B12-C81	A9-B12-C82	A9-B12-C83	A9-B12-C84
	A9-B12-C85	A9-B12-C86	A9-B12-C87	A9-B12-C88	A9-B12-C89	A9-B12-C90
	A9-B12-C91	A9-B12-C92	A9-B12-C93	A9-B12-C94	A9-B12-C95	A9-B12-C96
20	A9-B12-C97	A9-B12-C98	A9-B12-C99	A9-B12-C100	A9-B12-C101	A9-B12-C102
	A9-B12-C103	A9-B12-C104	A9-B12-C105	A9-B12-C106	A9-B12-C107	A9-B12-C108
,	A9-B12-C109	A9-B12-C110	A9-B12-C111	A9-B12-C112	A9-B12-C113	A9-B12-C114
	A9-B12-C115	A9-B12-C116	A9-B12-C117	A9-B12-C118	A9-B12-C119	A9-B12-C120
	A9-B12-C121	A9-B12-C122	A9-B12-C123	A9-B12-C124	A9-B12-C125	A9-B12-C126
25	A9-B12-C127	A9-B12-C128	A9-B12-C129	A9-B12-C130	A9-B12-C131	A9-B12-C132
	A9-B12-C133	A9-B12-C134	A9-B12-C135	A9-B12-C136	A9-B12-C137	A9-B12-C138
	A9-B12-C139	A9-B12-C140	BLANK	BLANK	BLANK	BLANK
	A9-B13-C1	A9-B13-C2	A9-B13-C3	A9-B13-C4	A9-B13-C5	A9-B13-C6
	A9-B13-C7	A9-B13-C8	A9-B13-C9	A9-B13-C10	A9-B13-C11	A9-B13-C12
30	A9-B13-C13	A9-B13-C14	A9-B13-C15	A9-B13-C16	A9-B13-C17	A9-B13-C18
	A9-B13-C19	A9-B13-C20	A9-B13-C21	A9-B13-C22	A9-B13-C23	A9-B13-C24
	A9-B13-C25	A9-B13-C26	A9-B13-C27	A9-B13-C28	A9-B13-C29	A9-B13-C30
	A9-B13-C31	A9-B13-C32	A9-B13-C33	A9-B13-C34	A9-B13-C35	A9-B13-C36
	A9-B13-C37	A9-B13-C38	A9-B13-C39	A9-B13-C40	A9-B13-C41	A9-B13-C42
35	A9-B13-C43	A9-B13-C44	A9-B13-C45	A9-B13-C46	A9-B13-C47	A9-B13-C48
	A9-B13-C49	A9-B13-C50	A9-B13-C51	A9-B13-C52	A9-B13-C53	A9-B13-C54
	A9-B13-C55	A9-B13-C56	A9-B13-C57	A9-B13-C58	A9-B13-C59	A9-B13-C60

	A9-B13-C61	A9-B13-C62	A9-B13-C63	A9-B13-C64	A9-B13-C65	A9-B13-C66
	A9-B13-C67	A9-B13-C68	A9-B13-C69	A9-B13-C70	A9-B13-C71	A9-B13-C72
	A9-B13-C73	A9-B13-C74	A9-B13-C75	A9-B13-C76	A9-B13-C77	A9-B13-C78
	A9-B13-C79	A9-B13-C80	A9-B13-C81	A9-B13-C82	A9-B13-C83	A9-B13-C84
5	A9-B13-C85	A9-B13-C86	A9-B13-C87	A9-B13-C88	A9-B13-C89	A9-B13-C90
	A9-B13-C91	A9-B13-C92	A9-B13-C93	A9-B13-C94	A9-B13-C95	A9-B13-C96
	A9-B13-C97	A9-B13-C98	A9-B13-C99	A9-B13-C100	A9-B13-C101	A9-B13-C102
	A9-B13-C103	A9-B13-C104	A9-B13-C105	A9-B13-C106	A9-B13-C107	A9-B13-C108
	A9-B13-C109	A9-B13-C110	A9-B13-C111	A9-B13-C112	A9-B13-C113	A9-B13-C114
10	A9-B13-C115	A9-B13-C116	A9-B13-C117	A9-B13-C118	A9-B13-C119	A9-B13-C120
	A9-B13-C121	A9-B13-C122	A9-B13-C123	A9-B13-C124	A9-B13-C125	A9-B13-C126
	A9-B13-C127	A9-B13-C128	A9-B13-C129	A9-B13-C130	A9-B13-C131	A9-B13-C132
	A9-B13-C133	A9-B13-C134	A9-B13-C135	A9-B13-C136	A9-B13-C137	A9-B13-C138
	A9-B13-C139	A9-B13-C140	BLANK	BLANK	BLANK	BLANK
15	A10-B1-C1	A10-B1-C2	A10-B1-C3	A10-B1-C4	A10-B1-C5	A10-B1-C6
	A10-B1-C7	A10-B1-C8	A10-B1-C9	A10-B1-C10	A10-B1-C11	A10-B1-C12
	A10-B1-C13	A10-B1-C14	A10-B1-C15	A10-B1-C16	A10-B1-C17	A10-B1-C18
	A10-B1-C19	A10-B1-C20	A10-B1-C21	A10-B1-C22	A10-B1-C23	A10-B1-C24
	A10-B1-C25	A10-B1-C26	A10-B1-C27	A10-B1-C28	A10-B1-C29	A10-B1-C30
20	A10-B1-C31	A10-B1-C32	A10-B1-C33	A10-B1-C34	A10-B1-C35	A10-B1-C36
	A10-B1-C37	A10-B1-C38	A10-B1-C39	A10-B1-C40	A10-B1-C41	A10-B1-C42
	A10-B1-C43	A10-B1-C44	A10-B1-C45	A10-B1-C46	A10-B1-C47	A10-B1-C48
	A10-B1-C49	A10-B1-C50	A10-B1-C51	A10-B1-C52	A10-B1-C53	A10-B1-C54
	A10-B1-C55	A10-B1-C56	A10-B1-C57	A10-B1-C58	A10-B1-C59	A10-B1-C60
25	A10-B1-C61	A10-B1-C62	A10-B1-C63	A10-B1-C64	A10-B1-C65	A10-B1-C66
	A10-B1-C67	A10-B1-C68	A10-B1-C69	A10-B1-C70	A10-B1-C71	A10-B1-C72
	A10-B1-C73	A10-B1-C74	A10-B1-C75	A10-B1-C76	A10-B1-C77	A10-B1-C78
	A10-B1-C79	A10-B1-C80	A10-B1-C81	A10-B1-C82	A10-B1-C83	A10-B1-C84
	A10-B1-C85	A10-B1-C86	A10-B1-C87	A10-B1-C88	A10-B1-C89	A10-B1-C90
30	A10-B1-C91	A10-B1-C92	A10-B1-C93	A10-B1-C94	A10-B1-C95	. A10-B1-C96
	A10-B1-C97	A10-B1-C98	A10-B1-C99	A10-B1-C100	A10-B1-C101	A10-B1-C102
	A10-B1-C103	A10-B1-C104	A10-B1-C105	A10-B1-C106	A10-B1-C107	A10-B1-C108
	A10-B1-C109	A10-B1-C110	A10-B1-C111	A10-B1-C112	A10-B1-C113	A10-B1-C114
	A10-B1-C115	A10-B1-C116	A10-B1-C117	A10-B1-C118	A10-B1-C119	A10-B1-C120
35	A10-B1-C121	A10-B1-C122	A10-B1-C123	A10-B1-C124	A10-B1-C125	A10-B1-C126
	A10-B1-C127	A10-B1-C128	A10-B1-C129	A10-B1-C130	A10-B1-C131	A10-B1-C132
	A10-B1-C133	A10-B1-C134	A10-B1-C135	A10-B1-C136	A10-B1-C137	A10-B1-C138

	A10-B1-C139	A10-B1-C140	BLANK	BLANK	BLANK	BLANK
	A10-B2-C1	A10-B2-C2	A10-B2-C3	A10-B2-C4	A10-B2-C5	A10-B2-C6
	A10-B2-C7	A10-B2-C8	A10-B2-C9	A10-B2-C10	A10-B2-C11	A10-B2-C12
	A10-B2-C13	A10-B2-C14	A10-B2-C15	A10-B2-C16	A10-B2-C17	A10-B2-C18
5	A10-B2-C19	A10-B2-C20	A10-B2-C21	A10-B2-C22	A10-B2-C23	A10-B2-C24
	A10-B2-C25	A10-B2-C26	A10-B2-C27	A10-B2-C28	A10-B2-C29	A10-B2-C30
	A10-B2-C31	A10-B2-C32	A10-B2-C33	A10-B2-C34	A10-B2-C35	A10-B2-C36
	A10-B2-C37	A10-B2-C38	A10-B2-C39	A10-B2-C40	A10-B2-C41	A10-B2-C42
	A10-B2-C43	A10-B2-C44	A10-B2-C45	A10-B2-C46	A10-B2-C47	A10-B2-C48
10	A10-B2-C49	A10-B2-C50	A10-B2-C51	A10-B2-C52	A10-B2-C53	A10-B2-C54
	A10-B2-C55	A10-B2-C56	A10-B2-C57	A10-B2-C58	A10-B2-C59	A10-B2-C60
	A10-B2-C61	A10-B2-C62	A10-B2-C63	A10-B2-C64	A10-B2-C65	A10-B2-C66
	A10-B2-C67	A10-B2-C68	A10-B2-C69	A10-B2-C70	A10-B2-C71	A10-B2-C72
	A10-B2-C73	A10-B2-C74	A10-B2-C75	A10-B2-C76	A10-B2-C77	A10-B2-C78
15	A10-B2-C79	A10-B2-C80	A10-B2-C81	A10-B2-C82	A10-B2-C83	A10-B2-C84
	A10-B2-C85	A10-B2-C86	A10-B2-C87	A10-B2-C88	A10-B2-C89	A10-B2-C90
	A10-B2-C91	A10-B2-C92	A10-B2-C93	A10-B2-C94	A10-B2-C95	A10-B2-C96
	A10-B2-C97	A10-B2-C98	A10-B2-C99	A10-B2-C100	A10-B2-C101	A10-B2-C102
	A10-B2-C103	A10-B2-C104	A10-B2-C105	A10-B2-C106	A10-B2-C107	A10-B2-C108
20	A10-B2-C109	A10-B2-C110	A10-B2-C111	A10-B2-C112	A10-B2-C113	A10-B2-C114
	A10-B2-C115	A10-B2-C116	A10-B2-C117	A10-B2-C118	A10-B2-C119	A10-B2-C120
	A10-B2-C121	A10-B2-C122	A10-B2-C123	A10-B2-C124	A10-B2-C125	A10-B2-C126
	A10-B2-C127	A10-B2-C128	A10-B2-C129	A10-B2-C130	A10-B2-C131	A10-B2-C132
	A10-B2-C133	A10-B2-C134	A10-B2-C135	A10-B2-C136	A10-B2-C137	A10-B2-C138
25	A10-B2-C139	A10-B2-C140	BLANK	BLANK	BLANK	BLANK
	A10-B3-C1	A10-B3-C2	A10-B3-C3	A10-B3-C4	A10-B3-C5	A10-B3-C6
	A10-B3-C7	A10-B3-C8	A10-B3-C9	A10-B3-C10	A10-B3-C11	A10-B3-C12
	A10-B3-C13	A10-B3-C14	A10-B3-C15	A10-B3-C16	A10-B3-C17	A10-B3-C18
	A10-B3-C19	A10-B3-C20	A10-B3-C21	A10-B3-C22	A10-B3-C23	A10-B3-C24
30	A10-B3-C25	A10-B3-C26	A10-B3-C27	A10-B3-C28	A10-B3-C29	A10-B3-C30
	A10-B3-C31	A10-B3-C32	A10-B3-C33	A10-B3-C34	A10-B3-C35	A10-B3-C36
	A10-B3-C37	A10-B3-C38	A10-B3-C39	A10-B3-C40	A10-B3-C41	A10-B3-C42
	A10-B3-C43	A10-B3-C44	A10-B3-C45	Å10-B3-C46	A10-B3-C47	A10-B3-C48
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	A10-B5-C139	A10-B5-C140	BLANK	BLANK	BLANK	BLANK
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	A10-B7-C103	A10-B7-C104	A10-B7-C105	A10-B7-C106	A10-B7-C107	A10-B7-C108
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	A10-B7-C139	A10-B7-C140	BLANK	BLANK	BLANK	BLANK
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	A10-B8-C139	A10-B8-C140	BLANK	BLANK	BLANK	BLANK
	A10-B9-C1	A10-B9-C2	A10-B9-C3	A10-B9-C4	A10-B9-C5	A10-B9-C6
	A10-B9-C7	A10-B9-C8	A10-B9-C9	A10-B9-C10	A10-B9-C11	A10-B9-C12
	A10-B9-C13	A10-B9-C14	A10-B9-C15	A10-B9-C16	A10-B9-C17	A10-B9-C18
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	A10-B9-C31	A10-B9-C32	A10-B9-C33	A10-B9-C34	A10-B9-C35	A10-B9-C36
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114.

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	A10-B9-C103	A10-B9-C104	A10-B9-C105	A10-B9-C106	A10-B9-C107	A10-B9-C108
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	A10-B9-C115	A10-B9-C116	A10-B9-C117	A10-B9-C118	A10-B9-C119	A10-B9-C120
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	A10-B9-C133	A10-B9-C134	A10-B9-C135	A10-B9-C136	A10-B9-C137	A10-B9-C138
	A10-B9-C139	A10-B9-C140	BLANK	BLANK	BLANK	BLANK
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	A10-B10-C13	A10-B10-C14	A10-B10-C15	A10-B10-C16	A10-B10-C17	A10-B10-C18
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	A10-B10-C43	A10-B10-C44	A10-B10-C45	A10-B10-C46	A10-B10-C47	A10-B10-C48
	A10-B10-C49	A10-B10-C50	A10-B10-C51	A10-B10-C52	A10-B10-C53	A10-B10-C54
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	A10-B10-C103	A10-B10-C104	A10-B10-C105	A10-B10-C106	A10-B10-C107	A10-B10-C108
	A10-B10-C109	A10-B10-C110	A10-B10-C111	A10-B10-C112	A10-B10-C113	A10-B10-C114
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	A10-B10-C133	A10-B10-C134	A10-B10-C135	A10-B10-C136	A10-B10-C137	A10-B10-C138
	A10-B10-C139	A10-B10-C140	BLANK	BLANK	BLANK	BLANK
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	A10-B11-C103	A10-B11-C104	A10-B11-C105	A10-B11-C106	A10-B11-C107	A10-B11-C108
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	A10-B11-C139	A10-B11-C140	BLANK	BLANK	BLANK	BLANK
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	A10-B12-C13	A10-B12-C14	A10-B12-C15	A10-B12-C16	A10-B12-C17	A10-B12-C18
	A10-B12-C19	A10-B12-C20	A10-B12-C21	A10-B12-C22	A10-B12-C23	A10-B12-C24
	A10-B12-C25	A10-B12-C26	A10-B12-C27	A10-B12-C28	A10-B12-C29	A10-B12-C30
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	A10-B12-C97	A10-B12-C98	A10-B12-C99	A10-B12-C100	A10-B12-C101	A10-B12-C102
	A10-B12-C103	A10-B12-C104	A10-B12-C105	A10-B12-C106	A10-B12-C107	A10-B12-C108

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	A10-B12-C139	A10-B12-C140	BLANK	BLANK	BLANK	BLANK
	A10-B13-C1	A10-B13-C2	A10-B13-C3	A10-B13-C4	A10-B13-C5	A10-B13-C6
	A10-B13-C7	A10-B13-C8	A10-B13-C9	A10-B13-C10	A10-B13-C11	A10-B13-C12
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	A10-B13-C25	A10-B13-C26	A10-B13-C27	A10-B13-C28	A10-B13-C29	A10-B13-C30
	A10-B13-C31	A10-B13-C32	A10-B13-C33	A10-B13-C34	A10-B13-C35	A10-B13-C36
	A10-B13-C37	A10-B13-C38	A10-B13-C39	A10-B13-C40	A10-B13-C41	A10-B13-C42
	A10-B13-C43	A10-B13-C44	A10-B13-C45	A10-B13-C46	A10-B13-C47	A10-B13-C48
15	A10-B13-C49	A10-B13-C50	A10-B13-C51	A10-B13-C52	A10-B13-C53	A10-B13-C54
	A10-B13-C55	A10-B13-C56	A10-B13-C57	A10-B13-C58	A10-B13-C59	A10-B13-C60
	A10-B13-C61	A10-B13-C62	A10-B13-C63	A10-B13-C64	A10-B13-C65	A10-B13-C66
	A10-B13-C67	A10-B13-C68	A10-B13-C69	A10-B13-C70	A10-B13-C71	A10-B13-C72
	A10-B13-C73	A10-B13-C74	A10-B13-C75	A10-B13-C76	A10-B13-C77	A10-B13-C78
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	A10-B13-C85	A10-B13-C86	A10-B13-C87	A10-B13-C88	A10-B13-C89	A10-B13-C90
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	A10-B13-C133	A10-B13-C134	A10-B13-C135	A10-B13-C136	A10-B13-C137	A10-B13-C138
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	A11-B1-C139	A11-B1-C140	BLANK	BLANK	BLANK	BLANK
	A11-B2-C1	A11-B2-C2	A11-B2-C3	A11-B2-C4	A11-B2-C5	A11-B2-C6
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	A11-B2-C55	A11-B2-C56	A11-B2-C57	A11-B2-C58	A11-B2-C59	A11-B2-C60
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	A11-B2-C115	A11-B2-C116	A11-B2-C117	A11-B2-C118	A11-B2-C119	A11-B2-C120

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	A11-B2-C127	A11-B2-C128	A11-B2-C129	A11-B2-C130	A11-B2-C131	A11-B2-C132
	A11-B2-C133	A11-B2-C134	A11-B2-C135	A11-B2-C136	A11-B2-C137	A11-B2-C138
	A11-B2-C139	A11-B2-C140	BLANK	BLANK	BLANK	BLANK
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	A11-B3-C7	A11-B3-C8	A11-B3-C9	A11-B3-C10	A11-B3-C11	A11-B3-C12
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	A11-B6-C85	A11-B6-C86	A11-B6-C87	A11-B6-C88	A11-B6-C89	A11-B6-C90
	A11-B6-C91	A11-B6-C92	A11-B6-C93	A11-B6-C94	A11-B6-C95	A11-B6-C96
	A11-B6-C97	A11-B6-C98	A11-B6-C99	A11-B6-C100	A11-B6-C101	A11-B6-C102
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	A11-B6-C109	A11-B6-C110	A11-B6-C111	A11-B6-C112	A11-B6-C113	A11-B6-C114
	A11-B6-C115	A11-B6-C116	A11-B6-C117	A11-B6-C118	A11-B6-C119	A11-B6-C120
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	A11-B6-C127	A11-B6-C128	A11-B6-C129	A11-B6-C130	A11-B6-C131	A11-B6-C132
25	A11-B6-C133	A11-B6-C134	A11-B6-C135	A11-B6-C136	A11-B6-C137	A11-B6-C138
	A11-B6-C139	A11-B6-C140	BLANK	BLANK	BLANK	BLANK
	A11-B7-C1	A11-B7-C2	A11-B7-C3	A11-B7-C4	A11-B7-C5	A11-B7-C6
	A11-B7-C7	A11-B7-C8	A11-B7-C9	A11-B7-C10	A11-B7-C11	A11-B7-C12
	A11-B7-C13	A11-B7-C14	A11-B7-C15	A11-B7-C16	A11-B7-C17	A11-B7-C18
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	A11-B7-C25	A11-B7-C26	A11-B7-C27	A11-B7-C28	A11-B7-C29	A11-B7-C30
	A11-B7-C31	A11-B7-C32	A11-B7-C33	A11-B7-C34	A11-B7-C35	A11-B7-C36
	A11-B7-C37	A11-B7-C38	A11-B7-C39	A11-B7-C40	A11-B7-C41	A11-B7-C42
	A11-B7-C43	A11-B7-C44	A11-B7-C45	A11-B7-C46	A11-B7-C47	A11-B7-C48
35	A11-B7-C49	A11-B7-C50	A11-B7-C51	A11-B7-C52	A11-B7-C53	A11-B7-C54
	A11-B7-C55	A11-B7-C56	A11-B7-C57	A11-B7-C58	A11-B7-C59	A11-B7-C60
	A11-B7-C61	A11-B7-C62	A11-B7-C63	A11-B7-C64	A11-B7-C65	A11-B7-C66

	A11-B7-C67	A11-B7-C68	A11-B7-C69	A11-B7-C70	A11-B7-C71	A11-B7-C72
	A11-B7-C73	A11-B7-C74	A11-B7-C75	A11-B7-C76	A11-B7-C77	A11-B7-C78
•	A11-B7-C79	A11-B7-C80	A11-B7-C81	A11-B7-C82	A11-B7-C83	A11-B7-C84
	A11-B7-C85	A11-B7-C86	A11-B7-C87	A11-B7-C88	A11-B7-C89	A11-B7-C90
5	A11-B7-C91	A11-B7-C92	A11-B7-C93	A11-B7-C94	A11-B7-C95	A11-B7-C96
	A11-B7-C97	A11-B7-C98	A11-B7-C99	A11-B7-C100	A11-B7-C101	A11-B7-C102
	A11-B7-C103	A11-B7-C104	A11-B7-C105	A11-B7-C106	A11-B7-C107	A11-B7-C108
	A11-B7-C109	A11-B7-C110	A11-B7-C111	A11-B7-C112	A11-B7-C113	A11-B7-C114
	A11-B7-C115	A11-B7-C116	A11-B7-C117	A11-B7-C118	A11-B7-C119	A11-B7-C120
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	A11-B7-C127	A11-B7-C128	A11-B7-C129	A11-B7-C130	A11-B7-C131	A11-B7-C132
	A11-B7-C133	A11-B7-C134	A11-B7-C135	A11-B7-C136	A11-B7-C137	A11-B7-C138
	A11-B7-C139	A11-B7-C140	BLANK	BLANK	BLANK	BLANK
	A11-B8-C1	A11-B8-C2	A11-B8-C3	A11-B8-C4	A11-B8-C5	A11-B8-C6
15	A11-B8-C7	A11-B8-C8	A11-B8-C9	A11-B8-C10	A11-B8-C11	A11-B8-C12
	A11-B8-C13	A11-B8-C14	A11-B8-C15	A11-B8-C16	A11-B8-C17	A11-B8-C18
	A11-B8-C19	A11-B8-C20	A11-B8-C21	A11-B8-C22	A11-B8-C23	A11-B8-C24
	A11-B8-C25	A11-B8-C26	A11-B8-C27	A11-B8-C28	A11-B8-C29	A11-B8-C30
٠	A11-B8-C31	A11-B8-C32	A11-B8-C33	A11-B8-C34	A11-B8-C35	A11-B8-C36
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	A11-B8-C43	A11-B8-C44	A11-B8-C45	A11-B8-C46	A11-B8-C47	A11-B8-C48
	A11-B8-C49	A11-B8-C50	A11-B8-C51	A11-B8-C52	A11-B8-C53	A11-B8-C54
	A11-B8-C55	A11-B8-C56	A11-B8-C57	A11-B8-C58	A11-B8-C59	A11-B8-C60
	A11-B8-C61	A11-B8-C62	A11-B8-C63	A11-B8-C64	A11-B8-C65	A11-B8-C66
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	A11-B8-C79	A11-B8-C80	A11-B8-C81	A11-B8-C82	A11-B8-C83	A11-B8-C84
	A11-B8-C85	A11-B8-C86	A11-B8-C87	A11-B8-C88	A11-B8-C89	A11-B8-C90
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	A11-B8-C103	A11-B8-C104	A11-B8-C105	A11-B8-C106	A11-B8-C107	A11-B8-C108
	A11-B8-C109	A11-B8-C110	A11-B8-C111	A11-B8-C112	A11-B8-C113	A11-B8-C114
	A11-B8-C115	A11-B8-C116	A11-B8-C117	A11-B8-C118	A11-B8-C119	A11-B8-C120
	A11-B8-C121	A11-B8-C122	A11-B8-C123	A11-B8-C124	A11-B8-C125	A11-B8-C126
35	A11-B8-C127	A11-B8-C128	A11-B8-C129	A11-B8-C130	A11-B8-C131	A11-B8-C132
	A11-B8-C133	A11-B8-C134	A11-B8-C135	A11-B8-C136	A11-B8-C137	A11-B8-C138
	A11-B8-C139	A11-B8-C140	BLANK	BLANK	BLANK	BLANK

	A11-B9-C1	A11-B9-C2	A11-B9-C3	A11-B9-C4	A11-B9-C5	A11-B9-C6
	A11-B9-C7	A11-B9-C8	A11-B9-C9	A11-B9-C10	A11-B9-C11	A11-B9-C12
	A11-B9-C13	A11-B9-C14	A11-B9-C15	A11-B9-C16	A11-B9-C17	A11-B9-C18
	A11-B9-C19	A11-B9-C20	A11-B9-C21	A11-B9-C22	A11-B9-C23	A11-B9-C24
5	A11-B9-C25	A11-B9-C26	A11-B9-C27	A11-B9-C28	A11-B9-C29	A11-B9-C30
	A11-B9-C31	A11-B9-C32	A11-B9-C33	A11-B9-C34	A11-B9-C35	A11-B9-C36
	A11-B9-C37	A11-B9-C38	A11-B9-C39	A11-B9-C40	A11-B9-C41	A11-B9-C42
	A11-B9-C43	A11-B9-C44	A11-B9-C45	A11-B9-C46	A11-B9-C47	A11-B9-C48
	A11-B9-C49	A11-B9-C50	A11-B9-C51	A11-B9-C52	A11-B9-C53	A11-B9-C54
10	A11-B9-C55	A11-B9-C56	A11-B9-C57	A11-B9-C58	A11-B9-C59	A11-B9-C60
	A11-B9-C61	A11-B9-C62	A11-B9-C63	A11-B9-C64	A11-B9-C65	A11-B9-C66
	A11-B9-C67	A11-B9-C68	A11-B9-C69	A11-B9-C70	A11-B9-C71	A11-B9-C72
	A11-B9-C73	A11-B9-C74	A11-B9-C75	A11-B9-C76	A11-B9-C77	A11-B9-C78
	A11-B9-C79	A11-B9-C80	A11-B9-C81	A11-B9-C82	A11-B9-C83	A11-B9-C84
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	A11-B9-C97	A11-B9-C98	A11-B9-C99	A11-B9-C100	A11-B9-C101	A11-B9-C102
	A11-B9-C103	A11-B9-C104	A11-B9-C105	A11-B9-C106	A1,1-B9-C107	A11-B9-C108
	A11-B9-C109	A11-B9-C110	A11-B9-C111	A11-B9-C112	A11-B9-C113	A11-B9-C114
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	A11-B9-C121	A11-B9-C122	A11-B9-C123	A11-B9-C124	A11-B9-C125	A11-B9-C126
	A11-B9-C127	A11-B9-C128	A11-B9-C129	A11-B9-C130	A11-B9-C131	A11-B9-C132
	A11-B9-C133	A11-B9-C134	A11-B9-C135	A11-B9-C136	A11-B9-C137	A11-B9-C138
	A11-B9-C139	A11-B9-C140	BLANK	BLANK	BLANK	BLANK
25	A11-B10-C1	A11-B10-C2	A11-B10-C3	A11-B10-C4	A11-B10-C5	A11-B10-C6
	A11-B10-C7	A11-B10-C8	A11-B10-C9	A11-B10-C10	A11-B10-C11	A11-B10-C12
	A11-B10-C13	A11-B10-C14	A11-B10-C15	A11-B10-C16	A11-B10-C17	A11-B10-C18
	A11-B10-C19	A11-B10-C20	A11-B10-C21	A11-B10-C22	A11-B10-C23	A11-B10-C24
	A11-B10-C25	A11-B10-C26	A11-B10-C27	A11-B10-C28	A11-B10-C29	A11-B10-C30
30	A11-B10-C31	A11-B10-C32	A11-B10-C33	A11-B10-C34	A11-B10-C35	A11-B10-C36
	A11-B10-C37	A11-B10-C38	A11-B10-C39	A11-B10-C40	A11-B10-C41	A11-B10-C42
	A11-B10-C43	A11-B10-C44	A11-B10-C45	A11-B10-C46	A11-B10-C47	A11-B10-C48
	A11-B10-C49	A11-B10-C50	A11-B10-C51	A11-B10-C52	A11-B10-C53	A11-B10-C54
	A11-B10-C55	A11-B10-C56	A11-B10-C57	A11-B10-C58	A11-B10-C59	A11-B10-C60
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	A11-B10-C67	A11-B10-C68	A11-B10-C69	A11-B10-C70	A11-B10-C71	A11-B10-C72
	A11-B10-C73	A11-B10-C74	A11-B10-C75	A11-B10-C76	A11-B10-C77	A11-B10-C78

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	A11-B10-C79	A11-B10-C80	A11-B10-C81	A11-B10-C82	A11-B10-C83	A11-B10-C84
	A11-B10-C85	A11-B10-C86	A11-B10-C87	A11-B10-C88	A11-B10-C89	A11-B10-C90
	A11-B10-C91	A11-B10-C92	A11-B10-C93	A11-B10-C94	A11-B10-C95	A11-B10-C96
	A11-B10-C97	A11-B10-C98	A11-B10-C99	A11-B10-C100	A11-B10-C101	A11-B10-C102
5	A11-B10-C103	A11-B10-C104	A11-B10-C105	A11-B10-C106	A11-B10-C107	A11-B10-C108
	A11-B10-C109	A11-B10-C110	A11-B10-C111	A11-B10-C112	A11-B10-C113	A11-B10-C114
	A11-B10-C115	A11-B10-C116	A11-B10-C117	A11-B10-C118	A11-B10-C119	A11-B10-C120
	A11-B10-C121	A11-B10-C122	A11-B10-C123	A11-B10-C124	A11-B10-C125	A11-B10-C126
	A11-B10-C127	A11-B10-C128	A11-B10-C129	A11-B10-C130	A11-B10-C131	A11-B10-C132
10	A11-B10-C133	A11-B10-C134	A11-B10-C135	A11-B10-C136	A11-B10-C137	A11-B10-C138
	A11-B10-C139	A11-B10-C140	BLANK	BLANK	BLANK	BLANK
	A11-B11-C1	A11-B11-C2	A11-B11-C3	A11-B11-C4	A11-B11-C5	A11-B11-C6
	A11-B11-C7	A11-B11-C8	A11-B11-C9	A11-B11-C10	A11-B11-C11	A11-B11-C12
	A11-B11-C13	A11-B11-C14	A11-B11-C15	A11-B11-C16	A11-B11-C17	A11-B11-C18
15	A11-B11-C19	A11-B11-C20	A11-B11-C21	A11-B11-C22	A11-B11-C23	A11-B11-C24
	A11-B11-C25	A11-B11-C26	A11-B11-C27	A11-B11-C28	A11-B11-C29	A11-B11-C30
	A11-B11-C31	A11-B11-C32	A11-B11-C33	A11-B11-C34	A11-B11-C35	A11-B11-C36
	A11-B11-C37	A11-B11-C38	A11-B11-C39	A11-B11-C40	A11-B11-C41	A11-B11-C42
	A11-B11-C43	A11-B11-C44	A11-B11-C45	A11-B11-C46	A11-B11-C47	A11-B11-C48
20	A11-B11-C49	A11-B11-C50	A11-B11-C51	A11-B11-C52	A11-B11-C53	A11-B11-C54
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	A11-B11-C61	A11-B11-C62	A11-B11-C63	A11-B11-C64	A11-B11-C65	A11-B11-C66
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25	A11-B11-C79	A11-B11-C80	A11-B11-C81	A11-B11-C82	A11-B11-C83	A11-B11-C84
	A11-B11-C85	A11-B11-C86	A11-B11-C87	A11-B11-C88	A11-B11-C89	A11-B11-C90
	A11-B11-C91	A11-B11-C92	A11-B11-C93	A11-B11-C94	A11-B11-C95	A11-B11-C96
	A11-B11-C97	A11-B11-C98	A11-B11-C99	A11-B11-C100	A11-B11-C101	A11-B11-C102
	A11-B11-C103	A11-B11-C104	A11-B11-C105	A11-B11-C106	A11-B11-C107	A11-B11-C108
30	A11-B11-C109	A11-B11-C110	A11-B11-C111	A11-B11-C112	A11-B11-C113	A11-B11-C114
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	A11-B11-C127	A11-B11-C128	A11-B11-C129	A11-B11-C130	A11-B11-C131	A11-B11-C132
	A11-B11-C133	A11-B11-C134	A11-B11-C135	A11-B11-C136	A11-B11-C137	A11-B11-C138
35	A11-B11-C139	A11-B11-C140	BLANK	BLANK	BLANK	BLANK
	A11-B12-C1	A11-B12-C2	A11-B12-C3	A11-B12-C4	A11-B12-C5	A11-B12-C6
	A11-B12-C7	A11-B12-C8	A11-B12-C9	A11-B12-C10	A11-B12-C11	A11-B12-C12

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	A11-B12-C19	A11-B12-C20	A11-B12-C21	A11-B12-C22	A11-B12-C23	A11-B12-C24
	A11-B12-C25	A11-B12-C26	A11-B12-C27	A11-B12-C28	A11-B12-C29	A11-B12-C30
	A11-B12-C31	A11-B12-C32	A11-B12-C33	A11-B12-C34	A11-B12-C35	A11-B12-C36
5	A11-B12-C37	A11-B12-C38	A11-B12-C39	A11-B12-C40	A11-B12-C41	A11-B12-C42
	A11-B12-C43	A11-B12-C44	A11-B12-C45	A11-B12-C46	A11-B12-C47	A11-B12-C48
	A11-B12-C49	A11-B12-C50	A11-B12-C51	A11-B12-C52	A11-B12-C53	A11-B12-C54
	A11-B12-C55	A11-B12-C56	A11-B12-C57	A11-B12-C58	A11-B12-C59	A11-B12-C60
	A11-B12-C61	A11-B12-C62	A11-B12-C63	A11-B12-C64	A11-B12-C65	A11-B12-C66
10	A11-B12-C67	A11-B12-C68	A11-B12-C69	A11-B12-C70	A11-B12-C71	A11-B12-C72
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	A11-B12-C79	A11-B12-C80	A11-B12-C81	A11-B12-C82	A11-B12-C83	A11-B12-C84
	A11-B12-C85	A11-B12-C86	A11-B12-C87	A11-B12-C88	A11-B12-C89	A11-B12-C90
	A11-B12-C91	A11-B12-C92	A11-B12-C93	A11-B12-C94	A11-B12-C95	A11-B12-C96
15	A11-B12-C97	A11-B12-C98	A11-B12-C99	A11-B12-C100	A11-B12-C101	A11-B12-C102
	A11-B12-C103	A11-B12-C104	A11-B12-C105	A11-B12-C106	A11-B12-C107	A11-B12-C108
	A11-B12-C109	A11-B12-C110	A11-B12-C111	A11-B12-C112	A11-B12-C113	A11-B12-C114
	A11-B12-C115	A11-B12-C116	A11-B12-C117	A11-B12-C118	A11-B12-C119	A11-B12-C120
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	A11-B12-C133	A11-B12-C134	A11-B12-C135	A11-B12-C136	A11-B12-C137	A11-B12-C138
	A11-B12-C139	A11-B12-C140	BLANK	BLANK	BLANK	BLANK
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	A11-B13-C7	A11-B13-C8	A11-B13-C9	A11-B13-C10	A11-B13-C11	A11-B13-C12
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	A11-B13-C25	A11-B13-C26	A11-B13-C27	A11-B13-C28	A11-B13-C29	A11-B13-C30
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	A11-B13-C133	A11-B13-C134	A11-B13-C135	A11-B13-C136	A11-B13-C137	A11-B13-C138
	A11-B13-C139	A11-B13-C140	BLANK	BLANK	BLANK	BLANK
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	A12-B1-C7	A12-B1-C8	A12-B1-C9	A12-B1-C10	A12-B1-C11	A12-B1-C12
	A12-B1-C13	A12-B1-C14	A12-B1-C15	A12-B1-C16	A12-B1-C17	A12-B1-C18
	A12-B1-C19	A12-B1-C20	A12-B1-C21	A12-B1-C22	A12-B1-C23	A12-B1-C24
	A12-B1-C25	A12-B1-C26	A12-B1-C27	A12-B1-C28	A12-B1-C29	A12-B1-C30
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	A12-B1-C49	A12-B1-C50	A12-B1-C51	A12-B1-C52	A12-B1-C53	A12-B1-C54
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	A12-B1-C79	A12-B1-C80	A12-B1-C81	A12-B1-C82	A12-B1-C83	A12-B1-C84
	A12-B1-C85	A12-B1-C86	A12-B1-C87	A12-B1-C88	A12-B1-C89	A12-B1-C90
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	A12-B1-C103	A12-B1-C104	A12-B1-C105	A12-B1-C106	A12-B1-C107	A12-B1-C108
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	A12-B1-C139	A12-B1-C140	BLANK	BLANK	BLANK	BLANK
	A12-B2-C1	A12-B2-C2	A12-B2-C3	A12-B2-C4	A12-B2-C5	A12-B2-C6
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	A12-B2-C19	A12-B2-C20	A12-B2-C21	A12-B2-C22	A12-B2-C23	A12-B2-C24

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	A12-B2-C31	A12-B2-C32	A12-B2-C33	A12-B2-C34	A12-B2-C35	A12-B2-C36
	A12-B2-C37	A12-B2-C38	A12-B2-C39	A12-B2-C40	A12-B2-C41	A12-B2-C42
	A12-B2-C43	A12-B2-C44	A12-B2-C45	A12-B2-C46	A12-B2-C47	A12-B2-C48
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	A12-B2-C61	A12-B2-C62	A12-B2-C63	A12-B2-C64	A12-B2-C65	A12-B2-C66
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	A12-B2-C133	A12-B2-C134	A12-B2-C135	A12-B2-C136	A12-B2-C137	A12-B2-C138
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	A12-B3-C7	A12-B3-C8	A12-B3-C9	A12-B3-C10	A12-B3-C11	A12-B3-C12
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	A12-B3-C19	A12-B3-C20	A12-B3-C21	A12-B3-C22	A12-B3-C23	A12-B3-C24
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	A12-B3-C73	A12-B3-C74	A12-B3-C75	A12-B3-C76	A12-B3-C77	A12-B3-C78
	· A12-B3-C79	A12-B3-C80	A12-B3-C81	A12-B3-C82	A12-B3-C83	A12-B3-C84
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	A12-B3-C97	A12-B3-C98	A12-B3-C99	A12-B3-C100	A12-B3-C101	A12-B3-C102

	A12-B3-C103	A12-B3-C104	A12-B3-C105	A12-B3-C106	A12-B3-C107	A12-B3-C108
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	A12-B3-C115	A12-B3-C116	A12-B3-C117	A12-B3-C118	A12-B3-C119	A12-B3-C120
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	A12-B3-C139	A12-B3-C140	BLANK	BLANK	BLANK	BLANK
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	A12-B4-C25	A12-B4-C26	A12-B4-C27	A12-B4-C28	A12-B4-C29	A12-B4-C30
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	A12-B4-C139	A12-B4-C140	BLANK	BLANK	BLANK	BLANK
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	A12-B5-C97	A12-B5-C98	A12-B5-C99	A12-B5-C100	A12-B5-C101	A12-B5-C102
	A12-B5-C103	A12-B5-C104	A12-B5-C105	A12-B5-C106	A12-B5-C107	A12-B5-C108
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	A12-B5-C115	A12-B5-C116	A12-B5-C117	A12-B5-C118	A12-B5-C119	A12-B5-C120
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	A12-B5-C127	A12-B5-C128	A12-B5-C129	A12-B5-C130	A12-B5-C131	A12-B5-C132
	A12-B5-C133	A12-B5-C134	A12-B5-C135	A12-B5-C136	A12-B5-C137	A12-B5-C138
	A12-B5-C139	A12-B5-C140	BLANK	BLANK	BLANK	BLANK
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	A12-B6-C13	A12-B6-C14	A12-B6-C15	A12-B6-C16	A12-B6-C17	A12-B6-C18
	A12-B6-C19	A12-B6-C20	A12-B6-C21	A12-B6-C22	A12-B6-C23	A12-B6-C24
	A12-B6-C25	A12-B6-C26	A12-B6-C27	A12-B6-C28	A12-B6-C29	A12-B6-C30
	A12-B6-C31	A12-B6-C32	A12-B6-C33	A12-B6-C34	A12-B6-C35	A12-B6-C36
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	A12-B6-C43	A12-B6-C44	A12-B6-C45	A12-B6-C46	A12-B6-C47	A12-B6-C48
	A12-B6-C49	A12-B6-C50	A12-B6-C51	A12-B6-C52	A12-B6-C53	A12-B6-C54
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	A12-B6-C133	A12-B6-C134	A12-B6-C135	A12-B6-C136	A12-B6-C137	A12-B6-C138
5	A12-B6-C139	A12-B6-C140	BLANK	BLANK	BLANK	BLANK
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	A12-B7-C7	A12-B7-C8	A12-B7-C9	A12-B7-C10	A12-B7-C11	A12-B7-C12
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	A12-B7-C127	A12-B7-C128	A12-B7-C129	A12-B7-C130	A12-B7-C131	A12-B7-C132
	A12-B7-C133	A12-B7-C134	A12-B7-C135	A12-B7-C136	A12-B7-C137	A12-B7-C138
	A12-B7-C139	A12-B7-C140	BLANK	BLANK	BLANK	BLANK
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	A12-B8-C19	A12-B8-C20	A12-B8-C21	A12-B8-C22	A12-B8-C23	A12-B8-C24
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	A12-B8-C61	A12-B8-C62	A12-B8-C63	A12-B8-C64	A12-B8-C65	A12-B8-C66
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	A12-B8-C139	A12-B8-C140	BLANK	BLANK	BLANK	BLANK
	A12-B9-C1	A12-B9-C2	A12-B9-C3	A12-B9-C4	A12-B9-C5	A12-B9-C6
	A12-B9-C7	A12-B9-C8	A12-B9-C9	A12-B9-C10	A12-B9-C11	A12-B9-C12
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	A12-B9-C127	A12-B9-C128	A12-B9-C129	A12-B9-C130	A12-B9-C131	A12-B9-C132
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	A12-B9-C139	A12-B9-C140	BLANK	BLANK	BLANK	BLANK
	A12-B10-C1	A12-B10-C2	A12-B10-C3	A12-B10-C4	A12-B10-C5	A12-B10-C6
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	A12-B10-C13	A12-B10-C14	A12-B10-C15	A12-B10-C16	A12-B10-C17	A12-B10-C18
	A12-B10-C19	A12-B10-C20	A12-B10-C21	A12-B10-C22	A12-B10-C23	A12-B10-C24
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	A12-B10-C139	A12-B10-C140	BLANK	BLANK	BLANK	BLANK
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	A12-B11-C121	A12-B11-C122	A12-B11-C123	A12-B11-C124	A12-B11-C125	A12-B11-C126
	A12-B11-C127	A12-B11-C128	A12-B11-C129	A12-B11-C130	A12-B11-C131	A12-B11-C132
	A12-B11-C133	A12-B11-C134	A12-B11-C135	A12-B11-C136	A12-B11-C137	A12-B11-C138
	A12-B11-C139	A12-B11-C140	BLANK	BLANK	BLANK	BLANK
15	A12-B12-C1	A12-B12-C2	A12-B12-C3	A12-B12-C4	A12-B12-C5	A12-B12-C6
	A12-B12-C7	A12-B12-C8	A12-B12-C9	A12-B12-C10	A12-B12-C11	A12-B12-C12
	A12-B12-C13	A12-B12-C14	A12-B12-C15	A12-B12-C16	A12-B12-C17	A12-B12-C18
	A12-B12-C19	A12-B12-C20	A12-B12-C21	A12-B12-C22	A12-B12-C23	A12-B12-C24
	A12-B12-C25	A12-B12-C26	A12-B12-C27	A12-B12-C28	A12-B12-C29	A12-B12-C30
20	A12-B12-C31	A12-B12-C32	A12-B12-C33	A12-B12-C34	A12-B12-C35	A12-B12-C36
	A12-B12-C37	A12-B12-C38	A12-B12-C39	A12-B12-C40	A12-B12-C41	A12-B12-C42
	A12-B12-C43	A12-B12-C44	A12-B12-C45	A12-B12-C46	A12-B12-C47	A12-B12-C48
	A12-B12-C49	A12-B12-C50	A12-B12-C51	A12-B12-C52	A12-B12-C53	A12-B12-C54
•	A12-B12-C55	A12-B12-C56	A12-B12-C57	A12-B12-C58	A12-B12-C59	A12-B12-C60
25	A12-B12-C61	A12-B12-C62	A12-B12-C63	A12-B12-C64	A12-B12-C65	A12-B12-C66
	A12-B12-C67	A12-B12-C68	A12-B12-C69	A12-B12-C70	A12-B12-C71	A12-B12-C72
	A12-B12-C73	A12-B12-C74	A12-B12-C75	A12-B12-C76	A12-B12-C77	A12-B12-C78
	A12-B12-C79	A12-B12-C80	A12-B12-C81	A12-B12-C82	A12-B12-C83	A12-B12-C84
	A12-B12-C85	A12-B12-C86	A12-B12-C87	A12-B12-C88	A12-B12-C89	A12-B12-C90
30	A12-B12-C91	A12-B12-C92	A12-B12-C93	A12-B12-C94	A12-B12-C95	A12-B12-C96
	A12-B12-C97	A12-B12-C98	A12-B12-C99	A12-B12-C100	A12-B12-C101	A12-B12-C102
	A12-B12-C103	A12-B12-C104	A12-B12-C105	A12-B12-C106	A12-B12-C107	A12-B12-C108
	A12-B12-C109	A12-B12-C110	A12-B12-C111	A12-B12-C112	A12-B12-C113	A12-B12-C114
	A12-B12-C115	A12-B12-C116	A12-B12-C117	A12-B12-C118	A12-B12-C119	A12-B12-C120
35	A12-B12-C121	A12-B12-C122	A12-B12-C123	A12-B12-C124	A12-B12-C125	A12-B12-C126
	A12-B12-C127	A12-B12-C128	A12-B12-C129	A12-B12-C130	A12-B12-C131	A12-B12-C132
	A12-B12-C133	A12-B12-C134	A12-B12-C135	A12-B12-C136	A12-B12-C137	A12-B12-C138

	A12-B12-C139	A12-B12-C140	BLANK	BLANK	BLANK	BLANK
	A12-B13-C1	A12-B13-C2	A12-B13-C3	A12-B13-C4	A12-B13-C5	A12-B13-C6
	A12-B13-C7	A12-B13-C8	A12-B13-C9	A12-B13-C10	A12-B13-C11	A12-B13-C12
	A12-B1 3- C13	A12-B13-C14	A12-B13-C15	A12-B13-C16	A12-B13-C17	A12-B13-C18
5	A12-B13-C19	A12-B13-C20	A12-B13-C21	A12-B13-C22	A12-B13-C23	A12-B13-C24
	A12-B13-C25	A12-B13-C26	A12-B13-C27	A12-B13-C28	A12-B13-C29	A12-B13-C30
	A12-B13-C31	A12-B13-C32	A12-B13-C33	A12-B13-C34	A12-B13-C35	A12-B13-C36
	A12-B13-C37	A12-B13-C38	A12-B13-C39	A12-B13-C40	A12-B13-C41	A12-B13-C42
	A12-B13-C43	A12-B13-C44	A12-B13-C45	A12-B13-C46	A12-B13-C47	A12-B13-C48
10	A12-B13-C49	A12-B13-C50	A12-B13-C51	A12-B13-C52	A12-B13-C53	A12-B13-C54
-	A12-B13-C55	A12-B13-C56	A12-B13-C57	A12-B13-C58	A12-B13-C59	A12-B13-C60
	A12-B13-C61	A12-B13-C62	A12-B13-C63	A12-B13-C64	A12-B13-C65	A12-B13-C66
	A12-B13-C67	A12-B13-C68	A12-B13-C69	A12-B13-C70	A12-B13-C71	A12-B13-C72
	A12-B13-C73	A12-B13-C74	A12-B13-C75	A12-B13-C76	A12-B13-C77	A12-B13-C78
15	A12-B13-C79	A12-B13-C80	A12-B13-C81	A12-B13-C82	A12-B13-C83	A12-B13-C84
	A12-B13-C85	A12-B13-C86	A12-B13-C87	A12-B13-C88	A12-B13-C89	A12-B13-C90
	A12-B13-C91	A12-B13-C92	A12-B13-C93	A12-B13-C94	A12-B13-C95	A12-B13-C96
	A12-B13-C97	A12-B13-C98	A12-B13-C99	A12-B13-C100	A12-B13-C101	A12-B13-C102
	A12-B13-C103	A12-B13-C104	A12-B13-C105	A12-B13-C106	A12-B13-C107	A12-B13-C108
20	A12-B13-C109	A12-B13-C110	A12-B13-C111	A12-B13-C112	A12-B13-C113	A12-B13-C114
	A12-B13-C115	A12-B13-C116	A12-B13-C117	A12-B13-C118	A12-B13-C119	A12-B13-C120
	A12-B13-C121	A12-B13-C122	A12-B13-C123	A12-B13-C124	A12-B13-C125	A12-B13-C126
	A12-B13-C127	A12-B13-C128	A12-B13-C129	A12-B13-C130	A12-B13-C131	A12-B13-C132
	A12-B13-C133	A12-B13-C134	A12-B13-C135	A12-B13-C136	A12-B13-C137	A12-B13-C138
25	A12-B13-C139	A12-B13-C140	BLANK	BLANK	BLANK	BLANK.

Thus, for example, in the above list the compound denoted as A1-B1-C1 is the product of the combination of group A1 in Table 1 and B1 in Table 2 and C1 in Table 3, namely

5 Preferred compounds of the invention are selected from:

3-[1-(5-phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine;

3-[1-(3-phenylethyl-benzoyl)-piperidin-4-yl]-benzylamine;

3-{1-[3-(4-hydroxyphenyl)ethyl-benzoyl]-piperidin-4-yl}-benzylamine;

3-{1-[3-(6-amino-pyridin-3-yl)ethyl-benzoyl]-piperidin-4-yl}-benzylamine;

3-[1-(5-phenylethyl-thiophene-2-carbonyl)-piperidin-4-yl]-benzylamine;

4-fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine;

4-methyl-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine;

3-[1-(indole-6-carbonyl)-piperidin-4-yl]-benzylamine;

4-(3-aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-4-carbonitrile

[4-(3-aminomethylphenyl)piperidin-1-yl]-(3,4-dichlorophenyl)methanone;

1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-methylsulfanyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate;

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-methylsulfanyl-6,7-dihydro-benzo[c]thiophen-1-yl)-methanone trifluoroacetate;

20 1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-ethylsulfanyl-6,6-dimethyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate;

1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-propylsulfanyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate;

 $1-\{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl\}-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl\}-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl\}-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl\}-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-isopropylsulfanyl-6, 7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-dihydro-7-$

benzo[c]thiophen-4-one trifluoroacetate;

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-benzo[b]thiophen-2-yl-methanone-trifluoroacetate;

- 1-[4-(3-Aminomethyl-phenyl)-4-hydroxy-piperidin-1-yl]-1-(5-phenethyl-pyridin-3-yl)-methanone-ditrifluoroacetate;
- 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(1-methyl-1H-indol-3-yl)-methanone-trifluoroacetate;
- 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(2-fluoro-phenylethynyl)-phenyl]-methanone
- 5 trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[2-(2-fluoro-phenyl)-ethyl]-phenyl}-methanone trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[2-(6-amino-pyridin-3-yl)-ethyl]-phenyl}-methanone tri-trifluoroacetate;
- 10 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(6-chloro-thieno[3,2-b]thiophen-2-yl)-methanone trifluoroacetate;
 - (3R,4S) and (3S, 4R)-4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester dihydrochloride;
 - 3-[1-(5-Phenylethynyl-furan-2-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate;
- 4-(3-Aminomethyl-phenyl)-piperidine-1-carboxylic acid (3,4-dichloro-phenyl)-amide trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(2,3-dihydro-benzofuran-5-yl)-methanone;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5,6-dichloro-pyridin-3-yl)-methanone;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-bromo-4-fluoro-phenyl)-methanone;
 - (E)-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-(2-nitro-phenyl)-propenone;
- 20 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-bromo-5-iodo-phenyl)-methanone;
 - (E)-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-phenyl-propenone;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-cyclohexyl-propan-1-one;

and the corresponding N-oxides, and their prodrugs; and pharmaceutically acceptable salts and solvates (e.g. hydrates) of such compounds and their N-oxides and prodrugs.

Pharmaceutical Compositions

As explained above, compounds of the present invention exhibit useful pharmacological activity and accordingly are incorporated into pharmaceutical compositions and used in the treatment of patients suffering from certain medical disorders. The present invention thus provides, according to a further aspect, compounds of the invention and pharmaceutical compositions containing compounds of the invention for use in therapy, wherein a pharmaceutical composition of the present invention comprising a compound of the present invention, and a pharmaceutically acceptable carrier thereof. As used herein, the term "pharmaceutically acceptable" preferably means approved by a regulatory agency of a government, in particular the Federal government or a state government, or listed in the U.S. Pharmacopeia or another generally recognized pharmacopeia for use in animals, and more

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particularly in humans. Suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin.

A pharmaceutical composition according to the present invention can be prepared according to the customary methods, using one or more pharmaceutically acceptable adjuvants or excipients. The adjuvants comprise, inter alia, diluents, sterile aqueous media and the various non-toxic organic solvents. The compositions may be presented in the form of tablets, pills, granules, powders, aqueous solutions or suspensions, injectable solutions, elixirs or syrups, and can contain one or more agents chosen from the group comprising sweeteners, flavorings, colorings, or stabilizers in order to obtain pharmaceutically acceptable preparations. The choice of vehicle and the content of active substance in the vehicle are generally determined in accordance with the solubility and chemical properties of the active compound, the particular mode of administration and the provisions to be observed in pharmaceutical practice. For example, excipients such as lactose, sodium citrate, calcium carbonate, dicalcium phosphate and disintegrating agents such as starch, alginic acids and certain complex silicates combined with lubricants such as magnesium stearate, sodium lauryl sulfate and talc may be used for preparing tablets. To prepare a capsule, it is advantageous to use lactose and high molecular weight polyethylene glycols. When aqueous suspensions are used they can contain emulsifying agents or agents which facilitate suspension. Diluents such as sucrose, ethanol, polyethylene glycol, propylene glycol, glycerol and chloroform or mixtures thereof may also be used. Such pharmaceutically acceptable carriers can also be sterile water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include mannitol, human serum albumin (HSA), starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, magnesium carbonate, magnesium stearate, sodium stearate, glycerol monostearate, tale, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. These compositions can take the form of solutions, suspensions, tablets, pills, capsules, powders, sustained-release formulations and the like.

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Naturally, a pharmaceutical composition of the present invention compositions will contain an effective diagnostic or therapeutic amount of the active compound together with a suitable amount of carrier so as to provide the form for proper administration to the patient. While intravenous injection is a very effective form of administration, other modes can be employed, such as by injection, or by oral, nasal or parenteral administration, which are discussed *infra*.

Methods of Treatment

Compounds within the scope of the present invention possess tryptase inhibition activity according to tests described in the literature and described in vitro procedures hereinafter, and which test results are believed to correlate to pharmacological activity in humans and other mammals. Thus, in a further embodiment, the present invention provides compounds of the invention and compositions containing compounds of the invention for use in the treatment of a patient suffering from, or subject to, conditions that can be ameliorated by the administration of an inhibitor of tryptase. For example, compounds of the present invention are useful in the treatment of inflammatory diseases, for example joint inflammation, including arthritis, rheumatoid arthritis and other arthritic conditions such as rheumatoid spondylitis, gouty arthritis, traumatic arthritis, rubella arthritis, psoriatic arthritis, osteoarthritis and other chronic inflammatory joint diseases, or diseases of joint cartilage destruction, ocular conjunctivitis, vernal conjunctivitis, inflammatory bowel disease, asthma, allergic rhinitis, interstitial lung diseases, fibrosis, sceleroderma, pulmonary fibrosis, liver cirrhosis, myocardial fibrosis, neurofibromas, hypertrophic scars, various dermatological conditions, for example, atopic dermatitis and psoriasis, myocardial infarction, stroke, angina and other consequences of atherosclerotic plaque rupture, as well as periodontal disease, diabetic retinopathy, tumor growth, anaphylaxis, multiple sclerosis, peptic ulcers, and syncytial viral infections.

A special embodiment of the therapeutic methods of the present invention is the treating of asthma.

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Another special embodiment of the therapeutic methods of the present invention is the treating of joint inflammation.

Another special embodiment of the therapeutic methods of the present invention is the treating of inflammatory bowel disease.

According to a further feature of the invention there is provided a method for the treatment of a human or animal patient suffering from, or subject to, conditions which can be ameliorated by the administration of an inhibitor of tryptase, for example conditions as hereinbefore described, which comprises the administration to the patient of an effective amount of compound of the invention or a composition containing a compound of the invention. "Effective amount" is meant to describe an amount of compound of the present invention effective in inhibiting tryptase and thus producing the desired therapeutic effect.

Combination Therapy

As explained above, other pharmaceutically active agents can be employed in combination with the compounds of the invention depending upon the disease being treated. For example, in the treatment

of asthma, beta-adrenergic agonists such as albuterol, terbutaline, formoterol, fenoterol or prenaline can be included, as can anticholinergics such as ipratropium bromide, anti-inflammatory corticosteroids such as beclomethasone dipropionate, triamcinolone acetonide, flunisolide or dexamethasone, and anti-inflammatory agents such as sodium cromoglycate and nedocromil sodium. Thus, the present invention extends to a pharmaceutical composition comprising a compound of the present invention and a second compound selected from the group consisting of a beta andrenergic agonist, an anticholinergic, an anti-inflammatory corticosteroid, and an anti-inflammatory agent; and a pharmaceutically acceptable carrier thereof. Particular pharmaceutical carriers having applications in this pharmaceutical composition are described herein.

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Furthermore, the present invention extends to a method for treating a patient suffering from asthma, comprising administering the patient a compound of the present invention, and a second compound selected from the group consisting of a beta andrenergic agonist, an anticholinergic, an anti-inflammatory corticosteroid, and an anti-inflammatory agent. In such a combination method, a compound of the present invention can be administered prior to the administration of the second compound, a compound of the present invention can be administered after administration of the second compound, or a compound of the present invention and the second compound can be administered concurrently.

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Modes of Delivery

According to the invention, a compound of the present invention, or a pharmaceutical composition of the present invention, may be introduced parenterally, transmucosally, e.g., orally, nasally, pulmonarily, or rectally, or transdermally to a patient.

25 Oral Delivery

Contemplated for use herein are oral solid dosage forms, which are described generally in Remington's Pharmaceutical Sciences, 18th Ed.1990 (Mack Publishing Co. Easton PA 18042) at Chapter 89, which is herein incorporated by reference. Solid dosage forms include tablets, capsules, pills, troches or lozenges, cachets or pellets. Also, liposomal or proteinoid encapsulation may be used to formulate the present compositions (as, for example, proteinoid microspheres reported in U.S. Patent No. 4,925,673). Liposomal encapsulation may be used and the liposomes may be derivatized with various polymers (e.g., U.S. Patent No. 5,013,556). A description of possible solid dosage forms for a therapeutic is given by Marshall, K. In: *Modern Pharmaceutics* Edited by G.S. Banker and C.T. Rhodes Chapter 10, 1979, herein incorporated by reference. In general, the formulation will include a compound of the present invention, and inert ingredients which allow for protection against the stomach environment, and release of the biologically active material, i.e., a compound of the present invention, in the intestine.

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Also specifically contemplated are oral dosage forms of a compound of the present invention. Such a compound may be chemically modified so that oral delivery is more efficacious. Generally, the chemical modification contemplated is the attachment of at least one moiety to the component molecule itself, where said moiety permits (a) inhibition of proteolysis; and (b) uptake into the blood stream from the stomach or intestine. Also desired is the increase in overall stability of the compound of the present invention, and increase in circulation time in the body. Examples of such moieties include: polyethylene glycol, copolymers of ethylene glycol and propylene glycol, carboxymethyl cellulose, dextran, polyvinyl alcohol, polyvinyl pyrrolidone and polyproline. Abuchowski and Davis, 1981, "Soluble Polymer-Enzyme Adducts" In: *Enzymes as Drugs*, Hocenberg and Roberts, eds., Wiley-Interscience, New York, NY, pp. 367-383; Newmark, et al., 1982, J. Appl. Biochem. 4:185-189. Other polymers that could be used are poly-1,3-dioxolane and poly-1,3,6-tioxocane. Preferred for pharmaceutical usage, as indicated above, are polyethylene glycol moieties.

For a compound of the present invention, the location of release may be the stomach, the small intestine (the duodenum, the jejunum, or the ileum), or the large intestine. One skilled in the art has available formulations that will not dissolve in the stomach, yet will release the material in the duodenum or elsewhere in the intestine. Preferably, the release will avoid the deleterious effects of the stomach environment, either by protection of the compound of the present invention, or by release of the compound beyond the stomach environment, such as in the intestine.

To ensure full gastric resistance a coating impermeable to at least pH 5.0 is essential. Examples of the more common inert ingredients that are used as enteric coatings are cellulose acetate trimellitate (CAT), hydroxypropylmethylcellulose phthalate (HPMCP), HPMCP 50, HPMCP 55, polyvinyl acetate phthalate (PVAP), Eudragit L30D, Aquateric, cellulose acetate phthalate (CAP), Eudragit L, Eudragit S, and shellac. These coatings may be used as mixed films.

A coating or mixture of coatings can also be used on tablets, which are not intended for protection against the stomach. This can include sugar coatings, or coatings that make the tablet easier to swallow. Capsules may consist of a hard shell (such as gelatin) for delivery of dry therapeutic i.e. powder; for liquid forms, a soft gelatin shell may be used. The shell material of cachets could be thick starch or other edible paper. For pills, lozenges, molded tablets or tablet triturates, moist massing techniques can be used.

The therapeutic can be included in the formulation as fine multi-particulates in the form of granules or pellets of particle size about 1 mm. The formulation of the material for capsule administration could

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also be as a powder, lightly compressed plugs or even as tablets. The therapeutic could be prepared by compression.

Colorants and flavoring agents may all be included. For example, the compound of the present invention may be formulated (such as by liposome or microsphere encapsulation) and then further contained within an edible product, such as a refrigerated beverage containing colorants and flavoring agents.

One may dilute or increase the volume of the therapeutic with an inert material. These diluents could include carbohydrates, especially mannitol, α-lactose, anhydrous lactose, cellulose, sucrose, modified dextrans and starch. Certain inorganic salts may be also be used as fillers including calcium triphosphate, magnesium carbonate and sodium chloride. Some commercially available diluents are Fast-Flo, Emdex, STA-Rx 1500, Emcompress and Avicell.

Disintegrants may be included in the formulation of the therapeutic into a solid dosage form. Materials used as disintegrates include, but are not limited to starch, including the commercial disintegrant based on starch, Explotab. Sodium starch glycolate, Amberlite, sodium carboxymethylcellulose, ultramylopectin, sodium alginate, gelatin, orange peel, acid carboxymethyl cellulose, natural sponge and bentonite may all be used. Another form of the disintegrants are the insoluble cationic exchange resins. Powdered gums may be used as disintegrants and as binders and these can include powdered gums such as agar, Karaya or tragacanth. Alginic acid and its sodium salt are also useful as disintegrants.

Binders may be used to hold the therapeutic agent together to form a hard tablet and include materials from natural products such as acacia, tragacanth, starch and gelatin. Others include methyl cellulose (MC), ethyl cellulose (EC) and carboxymethyl cellulose (CMC). Polyvinyl pyrrolidone (PVP) and hydroxypropylmethyl cellulose (HPMC) could both be used in alcoholic solutions to granulate the therapeutic.

An anti-frictional agent may be included in the formulation of the therapeutic to prevent sticking during the formulation process. Lubricants may be used as a layer between the therapeutic and the die wall, and these can include but are not limited to; stearic acid including its magnesium and calcium salts, polytetrafluoroethylene (PTFE), liquid paraffin, vegetable oils and waxes. Soluble lubricants may also be used such as sodium lauryl sulfate, magnesium lauryl sulfate, polyethylene glycol of various molecular weights, Carbowax 4000 and 6000.

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Glidants that might improve the flow properties of the drug during formulation and to aid rearrangement during compression might be added. The glidants may include starch, talc, pyrogenic silica and hydrated silicoaluminate.

- To aid dissolution of the therapeutic into the aqueous environment a surfactant might be added as a wetting agent. Surfactants may include anionic detergents such as sodium lauryl sulfate, dioctyl sodium sulfosuccinate and dioctyl sodium sulfonate. Cationic detergents might be used and could include benzalkonium chloride or benzethomium chloride. The list of potential non-ionic detergents that could be included in the formulation as surfactants are lauromacrogol 400, polyoxyl 40 stearate, polyoxyethylene hydrogenated castor oil 10, 50 and 60, glycerol monostearate, polysorbate 40, 60, 65 and 80, sucrose fatty acid ester, methyl cellulose and carboxymethyl cellulose. These surfactants could be present in the formulation of a compound of the present invention either alone or as a mixture in different ratios.
- Additives which potentially enhance uptake of a compound of the present invention are, for instance, the fatty acids oleic acid, linoleic acid and linolenic acid.

Controlled release oral formulation may be desirable. The drug could be incorporated into an inert matrix which permits release by either diffusion or leaching mechanisms, e.g., gums. Slowly degenerating matrices may also be incorporated into the formulation. Some enteric coatings also have a delayed release effect.

Another form of a controlled release of this therapeutic is by a method based on the Oros therapeutic system (Alza Corp.), i.e. the drug is enclosed in a semipermeable membrane which allows water to enter and push drug out through a single small opening due to osmotic effects.

Other coatings may be used for the formulation. These include a variety of sugars which could be applied in a coating pan. The therapeutic agent could also be given in a film coated tablet and the materials used in this instance are divided into 2 groups. The first are the nonenteric materials and include methyl cellulose, ethyl cellulose, hydroxyethyl cellulose, methylhydroxy-ethyl cellulose, hydroxypropyl cellulose, hydroxypropyl-methyl cellulose, sodium carboxy-methyl cellulose, providone and the polyethylene glycols. The second group consists of the enteric materials that are commonly esters of phthalic acid.

A mix of materials might be used to provide the optimum film coating. Film coating may be carried out in a pan-coater or in a fluidized bed or by compression coating.

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Pulmonary Delivery

Also contemplated herein is pulmonary delivery of a compound of the present invention, either alone, or in a pharmaceutical composition. The compound is delivered to the lungs of a mammal while inhaling and traverses across the lung epithelial lining to the blood stream. Other reports of this include Adjei et al., 1990, Pharmaceutical Research, 7:565-569; Adjei et al., 1990, International Journal of Pharmaceutics, 63:135-144 (leuprolide acetate); Braquet et al., 1989, Journal of Cardiovascular Pharmacology, 13(suppl. 5):143-146 (endothelin-1); Hubbard et al., 1989, Annals of Internal Medicine, Vol. III, pp. 206-212 (a1- antitrypsin); Smith et al., 1989, J. Clin. Invest. 84:1145-1146 (a-1-proteinase); Oswein et al., 1990, "Aerosolization of Proteins", Proceedings of Symposium on Respiratory Drug Delivery II, Keystone, Colorado, March, (recombinant human growth hormone); Debs et al., 1988, J. Immunol. 140:3482-3488 (interferon-γ and tumor necrosis factor alpha) and Platz et al., U.S. Patent No. 5,284,656 (granulocyte colony stimulating factor). A method and composition for pulmonary delivery of drugs for systemic effect is described in U.S. Patent No. 5,451,569, issued September 19, 1995 to Wong et al.

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Contemplated for use in the practice of this invention are a wide range of mechanical devices designed for pulmonary delivery of therapeutic products, including but not limited to nebulizers, metered dose inhalers, and powder inhalers, all of which are familiar to those skilled in the art.

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Some specific examples of commercially available devices suitable for the practice of this invention are the Ultravent nebulizer, manufactured by Mallinckrodt, Inc., St. Louis, Missouri; the Acorn II nebulizer, manufactured by Marquest Medical Products, Englewood, Colorado; the Ventolin metered dose inhaler, manufactured by Glaxo Inc., Research Triangle Park, North Carolina; and the Spinhaler powder inhaler, manufactured by Fisons Corp., Bedford, Massachusetts, to name only a few.

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All such devices require the use of formulations suitable for the dispensing a compound of the present invention. Typically, each formulation is specific to the type of device employed and may involve the use of an appropriate propellant material, in addition to the usual diluents, adjuvants and/or carriers useful in therapy. Also, the use of liposomes, microcapsules or microspheres, inclusion complexes, or other types of carriers is contemplated. Chemically modified compounds of the present invention may also be prepared in different formulations depending on the type of chemical modification or the type of device employed.

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Formulations suitable for use with a nebulizer, either jet or ultrasonic, will typically comprise a compound of the present invention dissolved in water at a concentration of about 0.1 to 25 mg of compound per mL of solution. The formulation may also include a buffer and a simple sugar (e.g., for stabilization and regulation of osmotic pressure). The nebulizer formulation may also contain a

surfactant, to reduce or prevent surface induced aggregation of the compound caused by atomization of the solution in forming the aerosol.

Formulations for use with a metered-dose inhaler device will generally comprise a finely divided powder containing a compound of the invention suspended in a propellant with the aid of a surfactant. The propellant may be any conventional material employed for this purpose, such as a chlorofluorocarbon, a hydrochlorofluorocarbon, a hydrofluorocarbon, or a hydrocarbon, including trichlorofluoromethane, dichlorodifluoromethane, dichlorotetrafluoroethanol, and 1,1,1,2-tetrafluoroethane, or combinations thereof. Suitable surfactants include sorbitan trioleate and soya lecithin. Oleic acid may also be useful as a surfactant.

Formulations for dispensing from a powder inhaler device will comprise a finely divided dry powder containing a compound of the invention, and may also include a bulking agent, such as lactose, sorbitol, sucrose, or mannitol in amounts which facilitate dispersal of the powder from the device, e.g., 50 to 90% by weight of the formulation. The compound of the present invention should most advantageously be prepared in particulate form with an average particle size of less than 10 mm (or microns), most preferably 0.5 to 5 mm, for most effective delivery to the distal lung.

Nasal Delivery

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Nasal delivery of a compound of the present invention is also contemplated. Nasal delivery allows the passage of the compound to the blood stream directly after administering the therapeutic product to the nose, without the necessity for deposition of the product in the lung. Formulations for nasal delivery include those with dextran or cyclodextran.

25 Transdermal Delivery

Various and numerous methods are known in the art for transdermal administration of a drug, e.g., via a transdermal patch, have applications in the present invention. Transdermal patches are described in for example, U.S. Patent No. 5,407,713, issued April 18, 1995 to Rolando et al.; U.S. Patent No. 5,352,456, issued October 4, 1004 to Fallon et al.; U.S. Patent No. 5,332,213 issued August 9, 1994 to D'Angelo et al.; U.S. Patent No. 5,336,168, issued August 9, 1994 to Sibalis; U.S. Patent No. 5,290,561, issued March 1, 1994 to Farhadieh et al.; U.S. Patent No. 5,254,346, issued October 19, 1993 to Tucker et al.; U.S. Patent No. 5,164,189, issued November 17, 1992 to Berger et al.; U.S. Patent No. 5,163,899, issued November 17, 1992 to Sibalis; U.S. Patent Nos. 5,088,977 and 5,087,240, both issued February 18, 1992 to Sibalis; U.S. Patent No. 5,008,110, issued April 16, 1991 to Benecke et al.; and U.S. Patent No. 4,921,475, issued May 1, 1990 to Sibalis, the disclosure of each of which is incorporated herein by reference in its entirety.

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It can be readily appreciated that a transdermal route of administration may be enhanced by use of a dermal penetration enhancer, e.g., such as enhancers described in U.S. Patent No. 5,164,189 (supra), U.S. Patent No. 5,008,110 (supra), and U.S. Patent No. 4,879,119, issued November 7, 1989 to Aruga et al., the disclosure of each of which is incorporated herein by reference in its entirety.

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Topical Administration

For topical administration, gels (water or alcohol based), creams or ointments containing compounds of the invention may be used. Compounds of the invention may also be incorporated in a gel or matrix base for application in a patch, which would allow a controlled release of compound through the transdermal barrier.

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Rectal Administration

Solid compositions for rectal administration include suppositories formulated in accordance with known methods and containing at least one compound of the invention.

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The percentage of active ingredient in the compositions of the invention may be varied, it being necessary that it should constitute a proportion such that a suitable dosage shall be obtained. Obviously, several unit dosage forms may be administered at about the same time. The dose employed will be determined by the physician, and depends upon the desired therapeutic effect, the route of administration and the duration of the treatment, and the condition of the patient. In the adult, the doses are generally from about 0.001 to about 50, preferably about 0.001 to about 5, mg/kg body weight per day by inhalation, from about 0.01 to about 100, preferably 0.1 to 70, more especially 0.5 to 10, mg/kg body weight per day by oral administration, and from about 0.001 to about 10, preferably 0.01 to 1, mg/kg body weight per day by intravenous administration. In each particular case, the doses will be determined in accordance with the factors distinctive to the subject to be treated, such as age, weight, general state of health and other characteristics which can influence the efficacy of the medicinal product.

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Furthermore, compounds according to the invention may be administered as frequently as necessary in order to obtain the desired therapeutic effect. Some patients may respond rapidly to a higher or lower dose and may find much weaker maintenance doses adequate. For other patients, it may be necessary to have long-term treatments at the rate of 1 to 4 doses per day, in accordance with the physiological requirements of each particular patient. Generally, the active product may be administered orally 1 to 4 times per day. Of course, for some patients, it will be necessary to prescribe not more than one or two doses per day.

Naturally, a patient in whom administration of a compound of the present invention is an effective therapeutic regimen is preferably a human, but can be any animal. Thus, as can be readily appreciated by one of ordinary skill in the art, the methods and pharmaceutical compositions of the present invention are particularly suited to administration to any animal, particularly a mammal, and including, but by no means limited to, domestic animals, such as feline or canine subjects, farm animals, such as but not limited to bovine, equine, caprine, ovine, and porcine subjects, wild animals (whether in the wild or in a zoological garden), research animals, such as mice, rats, rabbits, goats, sheep, pigs, dogs, cats, etc., avian species, such as chickens, turkeys, songbirds, etc., i.e., for veterinary medical use.

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Preparation of Compounds of the Invention

Compounds of the invention may be prepared by the application or adaptation of known methods, by which is meant methods used heretofore or described in the literature, for example those described by R.C.Larock in Comprehensive Organic Transformations, VCH publishers, 1989.

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In the reactions described hereinafter it may be necessary to protect reactive functional groups, for example hydroxy, amino, imino, thio or carboxy groups, where these are desired in the final product, to avoid their unwanted participation in the reactions. Conventional protecting groups may be used in accordance with standard practice, for examples see T.W. Greene and P.G.M.Wuts in "Protective Groups in Organic Chemistry" John Wiley and Sons, 1991.

Compounds of formula (Ia) wherein R³, R⁴, R⁵ and n are as hereinbefore defined, R¹ and R² are both hydrogen and is a single bond, represented by formula (IX), may be prepared as shown in Scheme 1

ö

Scheme 1

- 5 For example compounds of formula (IX) may be prepared by:-
 - (i) treating compounds of formula (II) wherein R⁴ and n are as hereinbefore defined and P¹ is a suitable protecting group, such as benzyloxycarbonyl, with a suitable base, such as lithium hexamethyldisilazane, in an inert solvent, such as tetrahydrofuran, and at a temperature at about -78°C, followed by reaction with N-phenyltrifluoromethane-sulfonimide to give compounds of formula (III) wherein R⁴, P¹ and n are as hereinbefore defined and Tf is -SO₂CF₃;
 - (ii) reaction of triflates of formula (III) with an aryl boronic acid of formula (X):-

in the presence of an aqueous base such as sodium bicarbonate and a palladium catalyst such as palladium tetrakistriphenylphosphine, and at a temperature from about 80 to about 100°C, to give compounds of formula (IV) wherein R⁴, R⁵, P¹ and n are as hereinbefore defined;

- (iii) reduction of compounds of formula (IV) with sodium borohydride in ethanol to give compounds of formula(V) wherein R⁴, R⁵, P¹ and are as hereinbefore defined;
- (iv) conversion of the hydroxymethyl group in compounds of formula (V) to an aminomethyl group which is suitably protected to facilitate the further processes described hereinafter for example reaction of compounds of formula (V) with phosphorus tribromide in pyridine followed by treatment of the resultant bromomethyl intermediate with di-tert-butyliminodicarboxylate to give compounds of formula (VI) wherein R⁴, R⁵, P¹ and n are as hereinbefore defined and P² and P³ are each tertiary-butyloxycarbonyl (a suitable protecting group that is stable under conditions for the subsequent removal of protecting group P¹);
 - (v) removal of the protecting group P¹ in compounds of formula (VI), for example when P¹ is benzyloxycarbonyl and P² and P³ are both tertiary-butyloxycarbonyl, the deprotection may conveniently be carried out by hydrogenation in the presence of a suitable metal catalyst, e.g. platinum or palladium optionally supported on an inert carrier such as carbon, preferably in a solvent such as methanol or ethanol to give compounds of formula (VII) wherein R⁴, R⁵ and n are as hereinbefore defined and P² and P³ are as just defined;
 - (vi) reaction of compounds of formula (VII) with compounds of formula (XI):-

$$\begin{array}{c|c}
O \\
| \\
R^3 - C - X^1
\end{array} (XI)$$

wherein R^3 is as hereinbefore defined and X^1 is a hydroxy group, or a halogen, preferably chlorine, atom using standard coupling conditions [for example when X^1 is a hydroxy group

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the reaction may be carried out using standard peptide coupling procedures for example coupling in the presence of O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate and triethylamine (or diisopropylethylamine) in tetrahydrofuran (or dimethylformamide), at room temperature; and when X^1 is a halogen atom the acylation reaction may be carried out with the aid of a base, such pyridine, preferably in a solvent such as tetrahydrofuran and at a temperature at about room temperature] to give compounds of formula (VIII) wherein R^3 , R^4 , R^5 , n, P^2 and P^3 are as defined above;

(vii) removal of the protecting groups P² and P³ in compounds of formula (VIII), for example when P² and P³ are both tertiary-butyloxycarbonyl the reaction may conveniently be carried out in the presence of an acid such as trifluoracetic acid in an inert solvent, such as dichloromethane, or by treatment with hydrogen chloride in methanol.

Compounds of formula (Ia) wherein R¹, R², R³, R⁴, R⁵ and n are as hereinbefore defined and is a single bond, represented by formula (XVI), may be prepared as shown in scheme 2.

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$$R^{4} \qquad (CH_{2})_{n}$$

$$R^{4} \qquad (CH_{2})_{n}$$

$$R^{5} \qquad (XIII)$$

$$R^{5} \qquad (XIII)$$

$$R^{5} \qquad (XIV)$$

$$R^{4} \qquad (CH_{2})_{n}$$

$$R^{5} \qquad (XIV)$$

Scheme 2

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For example compounds of formula (XVI) may be prepared by:-

(i) reaction of compounds of formula (II) wherein R⁴ and n are as hereinbefore defined and P¹ is a suitable protecting group, such as benzyloxycarbonyl, with an aryl boronate of formula (XVII):-

$$\mathbb{R}^1$$
 \mathbb{R}_2 $\mathbb{R}^2 \mathbb{P}^3$ (XVII)

wherein R¹, R², P² and P³ are as hereinbefore defined in the presence of potassium carbonate and a palladium catalyst such as [1,1'-bis-(diphenylphosphino)ferroceno]-dichloropalladium (II)-dichloromethane complex in an inert solvent, such as dimethylsulfoxide, and at a temperature at about 80°C to give compounds of formula (XII) wherein R¹, R², R⁴, R⁵, n, P¹, P² and P³ are as hereinbefore defined; alternatively compounds of formula (XII) may be prepared by reaction of compounds of formula (II) with bis(pinacolato)boron in the presence of potassium acetate, (diphenylphosphino)-ferrocene and [1,1'-bis-(diphenylphosphino)ferroceno]-dichloropalladium (II), in an inert solvent, such as dioxane, and at a temperature at about 80°C followed by reaction of the intermediate boronate of formula (XIII) with compounds of formula (XVIII):-

$$\begin{array}{c}
\mathbf{Br} \\
\mathbf{R}^{1} \\
\mathbf{R}^{2}
\end{array}$$
(XVIII)

wherein R¹, R², P¹ and P² are as hereinbefore defined in the presence of potassium carbonate and a palladium catalyst such as [1,1'-bis-(diphenylphosphino)ferroceno]-dichloropalladium (II)-dichloromethane complex in an inert solvent, such as dimethylsulfoxide, and at a temperature at about 80°C];

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(ii) removal of the protecting group P¹ in compounds of formula (XII), for example when P¹ is benzyloxycarbonyl and P² and P³ are both tertiary-butyloxycarbonyl, the deprotection may conveniently be carried out by hydrogenation as described hereinabove to give compounds of formula (XIV) wherein R¹, R², R⁴, R⁵, n, P² and P³ are as just defined;

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- (iii) reaction of compounds of formula (XIV) with compounds of formula (XI) wherein R¹ is as hereinbefore defined and X¹ is a hydroxy group, or a halogen, preferably chlorine, atom using standard coupling conditions [for example those described hereinabove] to give compounds of formula (XV) wherein R¹, R², R³, R⁴, R⁵, n, P² and P³ are as defined above;
- (vii) removal of the protecting groups P² and P³ in compounds of formula (XV), using standard coupling conditions [for example those described hereinabove].
- Compounds of formula (Ia) wherein R¹, R², R³, R⁴, R⁵ and n are as hereinbefore defined and

 is a single bond, represented by formula (XVI), may also be prepared using resin technology as shown in scheme 3:-

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For example compounds of formula (XVI) may be prepared by:-

Coupling of the resin (XIX, an aminomethylated styrene/divinylbenzene copolymer), where represents the polymeric core (comprising polystyrene crosslinked with 1% to 2% divinylbenzene), with 4-hydroxy-2,3,5,6-tetrafluorobenzoic acid, according to the

Scheme 3

procedure described by J.M.Salvino et. al. in International Patent Application Publication No. WO 99/67228, to give TFP resin wherein p is as hereinbefore defined;

- (ii) treatment of TFP resin with acids of formula (XI) wherein R³ is as hereinbefore defined and X¹ is hydroxy, in the presence of diisopropyl carbodiimide and dimethylaminopyridine, in an inert solvent, such as dimethylformamide, and at a temperature at about room temperature, to give resin 1 wherein R³ and P are hereinbefore defined;
- (iii) treatment of resin 1 with compounds of formula (XIV) wherein R¹, R², R⁴, R⁵, n, P¹ and P² are as defined immediately hereinbefore, in an inert solvent, such as dichloromethane, and at a temperature at about room temperature, to give compounds of formula (XV);
- (iv) removal of the protecting groups in compounds of formula (XV), for example when P² and P³ are both tertiary-butyloxycarbonyl the reaction may conveniently be carried out in the presence of an acid such as trifluoracetic acid in an inert solvent, such as dichloromethane, or by treatment with hydrogen chloride in methanol.

Compounds of formula (Ib), wherein R³ and R⁵ are as hereinbefore defined and R⁴ is cyano attached at the 4 position of the piperidine ring, represented by formula (XX), may be prepared as shown in scheme 4:-

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$$(XXII)$$

$$(XXIII)$$

$$(XXIII)$$

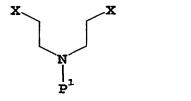
$$P^{2}NH$$
 $P^{2}NH$
 $P^{2}NH$

For example compounds of formula (XX) may be prepared by:-

Searching a benzyl bromide of formula (XXI) wherein R⁵ is as hereinbefore defined, with sodium cyanide, in the presence of a phase transfer catalyst, such as tetrabutylammonium bromide, in a mixture of water and an inert solvent, such as dichloromethane, and at a temperature at about room temperature to give compounds of formula (XXII) wherein R⁵ is as hereinbefore defined;

Scheme 4

(ii) treatment of the benzylcyanides of formula (XXII) with a suitably protected bis-(2-haloethyl)amine of formula (XXVIII):-



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wherein X is halo, preferably chloro, and P^1 is a suitable protecting group, such as tertiary-butyloxycarbonyl, in the presence of sodium hydride and in an inert solvent, such as dimethylformamide, and at a temperature at about room temperature, to give compounds of formula (XXIII) wherein R^5 and P^1 are as hereinbefore defined;

(XXVIII)

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 (iii) hydrogenation of compounds of formula (XXIII) in the presence of hydrochloric acid in ethanol and under pressure to give compounds of formula (XXIV) wherein R⁵ and P¹ are as hereinbefore defined;

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(iv) protection of the amino group in compounds of formula (XXIV) with a suitable protecting group, for example with a benzyloxycarbonyl group, to give compounds of formula (XXV) wherein R⁵, P¹ and P² are as hereinbefore defined;

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 (v) removal of the protecting group P¹ in compounds of formula (XXV) to give compounds of formula (XXVI) wherein R⁵ and P² are as hereinbefore defined;

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(vi) reaction of compounds of formula (XXVI) with compounds of formula (XI) wherein R¹ is as hereinbefore defined and X¹ is a hydroxy group, or a halogen, preferably chlorine, atom using standard coupling conditions [for example those described hereinabove] to give compounds of formula (XXVII) wherein R⁵ and P² are as defined above;

(vii) removal of the protecting groups P² in compounds of formula (XXVII), using standard coupling conditions [for example those described hereinabove].

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Compounds of formula (Ia) wherein R³, R⁴, R⁵ and n are as hereinbefore defined, R¹ and R² are both hydrogen and _____ is a double bond, represented by formula (IX), may be prepared by removal of the P¹ protecting group in compounds of formula (VI) followed by acylation with compounds of formula (XI) and subsequent removal of the P² and P³ protecting groups.

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Compounds of formula (Ia) wherein R¹, R², R³, R⁴, R⁵ and n are as hereinbefore defined and
is a double bond, represented by formula (XVI), may be prepared by removal of the P¹
protecting group in compounds of formula (XII) followed by acylation with compounds of formula
(XI) and subsequent removal of the P² and P³ protecting groups.

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According to a further feature of the present invention, compounds of the invention may be prepared by interconversion of other compounds of the invention.

As an example of the interconversion process, compounds of formula (Ia) wherein R¹, R², R⁴, R⁵ and n are as hereinbefore defined and R³ contains an optionally substituted alkylene linkage, may be prepared by hydrogenation of the corresponding compounds of formula (Ia) in which R³ contains the corresponding optionally substituted alkenylene or alkynylene linkage. The hydrogenation may be carried out using hydrogen (optionally under pressure) in the presence of a suitable metal catalyst, e.g. platinum or palladium optionally supported on an inert carrier such as carbon, preferably in a solvent such as methanol or ethanol, and at a temperature at about room temperature.

As another example of the interconversion process, compounds of the invention containing a heterocyclic group wherein the heteroatom is a nitrogen atom may be oxidized to their corresponding N-oxides. The oxidation may conveniently be carried out by means of reaction with a mixture of hydrogen peroxide and an organic acid, e.g. acetic acid, preferably at or above room temperature, for example at a temperature of about 60-90°C. Alternatively, the oxidation may be carried out by reaction with a peracid, for example peracetic acid or m-chloroperoxybenzoic acid, in an inert solvent such as chloroform or dichloromethane, at a temperature from about room temperature to reflux, preferably at elevated temperature. The oxidation may alternatively be carried out by reaction with hydrogen peroxide in the presence of sodium tungstate at temperatures between room temperature and about 60°C.

As another example of the interconversion process, compounds of formula (Ia) containing sulfone linkages may be prepared by the oxidation of corresponding compounds containing -S- or sulfoxide linkages. For example, the oxidation may conveniently be carried out by means of reaction with a

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peroxyacid, e.g. 3-chloroperbenzoic acid, preferably in an inert solvent, e.g. dichloromethane, preferably at or near room temperature.

It will be appreciated that compounds of the present invention may contain asymmetric centers. These asymmetric centers may independently be in either the R or S configuration. It will be apparent to those skilled in the art that certain compounds of the invention may also exhibit geometrical isomerism. It is to be understood that the present invention includes individual geometrical isomers and stereoisomers and mixtures thereof, including racemic mixtures, of compounds the present invention. Such isomers can be separated from their mixtures, by the application or adaptation of known methods, for example chromatographic techniques and recrystallisation techniques, or they are separately prepared from the appropriate isomers of their intermediates.

According to a further feature of the invention, acid addition salts of the compounds of this invention may be prepared by reaction of the free base with the appropriate acid, by the application or adaptation of known methods. For example, the acid addition salts of the compounds of this invention may be prepared either by dissolving the free base in water or aqueous alcohol solution or other suitable solvents containing the appropriate acid and isolating the salt by evaporating the solution, or by reacting the free base and acid in an organic solvent, in which case the salt separates directly or can be obtained by concentration of the solution.

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The acid addition salts of the compounds of this invention can be regenerated from the salts by the application or adaptation of known methods. For example, parent compounds of the invention can be regenerated from their acid addition salts by treatment with an alkali, e.g. aqueous sodium bicarbonate solution or aqueous ammonia solution.

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The starting materials and intermediates may be prepared by the application or adaptation of known methods, for example methods as described in the Reference Examples or their obvious chemical equivalents.

Aryl boronates of formula (XVII) wherein R¹, R², P² and P³ are as hereinbefore defined may be prepared by reaction of compounds of formula (XVIII) wherein R¹, R², P² and P³ are as hereinbefore defined, with bis(pinacolato)boron in the presence of potassium acetate and [1,1'-bis-

(diphenylphosphino)ferroceno]-dichloropalladium (II) in an inert solvent, such as dioxane, at and at a temperature at about 80°C.

Compounds of formula (XVIII) wherein R¹ and R² are as hereinbefore defined and P² and P³ are both tertiary-butoxycarbonyl may be prepared by reaction of compounds of formula (XXIX):-

$$R^1$$
 R_2 $(XXIX)$

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wherein R¹ and R² are as hereinbefore defined with sodium hydride and di-tertiarybutyliminodicarboxylate, in an inert solvent, such as tetrahydrofuran, and at a temperature at about room temperature.

Intermediates of formulae (VIII) and (XV) are novel compounds and, as such, they and their processes described herein for their preparation constitute further features of the present invention.

The present invention is further Exemplified but not limited by the following illustrative Examples and Reference Examples.

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In the nuclear magnetic resonance spectra (NMR) the chemical shifts are expressed in ppm relative to tetramethylsilane. Abbreviations have the following significances: br = broad, dd = double doublet, s = singlet; m = multiplet.

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High Pressure Liquid Chromatography/ Mass Spectrometry (LC-MS) conditions for determination of retention times (R_T) were as follows: 3 micron Luna C18 (2) HPLC column (30mm x 4.6mm) eluting with (i) mixture of 0.05% trifluoroacetic acid in acetonitrile and 0.05% trifluoroacetic acid in water (1:19, v/v) for 2 minutes, (ii) mixture of 0.05% trifluoroacetic acid in acetonitrile and 0.05% trifluoroacetic acid in water (1:19 to 19:1, v/v) gradient elution over 10 minutes, (iii) mixture of 0.05% trifluoroacetic acid in acetonitrile and 0.05% trifluoroacetic acid in water (19:1, v/v) for 2 minutes, (iv) mixture of 0.05% trifluoroacetic acid in acetonitrile and 0.05% trifluoroacetic acid in water (1:19 to 1:19, v/v) gradient elution over 2 minutes; flow rate 2ml/minute with approximately 200µl/minute split to the Mass Spectrometer; injection volume 10-40µl; in line Diode Array (220-450nm), in line Evaporative light scattering (ELS) detection ELS - temperature 50°C, Gain 8 -

30 1.8ml/minute; Source temperature 150°C.

The present invention may be better understood by reference to the following non-limiting Examples, which are provided as exemplary of the invention. The following examples are presented in order to more fully illustrate particular embodiments of the invention. They should in no way be construed, however, as limiting the broad scope of the invention.

In the nuclear magnetic resonance spectra (NMR), reported infra, the chemical shifts are expressed in ppm relative to tetramethylsilane. Abbreviations have the following significances: br = broad, dd = double doublet, s = singlet; m = multiplet.

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Moreover, in the Examples, High Pressure Liquid Chromatography/ Mass Spectrometry (LC-MS) conditions for determination of retention times (R_T) were as follows: 3 micron Luna C18 (2) HPLC column (30mm x 4.6mm) eluting with (i) mixture of 0.05% trifluoroacetic acid in acetonitrile and 0.05% trifluoroacetic acid in water (1:19, v/v) for 2 minutes, (ii) mixture of 0.05% trifluoroacetic acid in acetonitrile and 0.05% trifluoroacetic acid in water (1:19 to 19:1, v/v) gradient elution over 10 minutes, (iii) mixture of 0.05% trifluoroacetic acid in acetonitrile and 0.05% trifluoroacetic acid in water (19:1, v/v) for 2 minutes, (iv) mixture of 0.05% trifluoroacetic acid in acetonitrile and 0.05% trifluoroacetic acid in water (1:19 to 1:19, v/v) gradient elution over 2 minutes; flow rate 2ml/minute with approximately 200μl/minute split to the Mass Spectrometer; injection volume 10-40μl; in line Diode Array (220-450nm), in line Evaporative light scattering (ELS) detection ELS - temperature 50°C, Gain 8 - 1.8ml/minute; Source temperature 150°C.

EXAMPLE 1

3-[1-(5-Phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(5-phenylethynyl-pyridin-3-yl)-methanone) di-hydrochloride)

A. B-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-pinacolato-boron

A solution of 3-bromobenzylbromide (7.5g, 30mmol) and di-tert-butyliminodicarboxylate (6.5g, 30mmol) in anhydrous tetrahydrofuran (80ml) was treated portionwise with sodium hydride (1.2g, 60% dispersion in mineral oil). After stirring at ambient temperature for 7 hours the reaction mixture was partitioned between saturated aqueous ammonium chloride solution (90ml) and ethyl acetate (2 lots of 250ml). The combined organic layers were washed with brine (75ml), then dried over magnesium sulfate and then concentrated under vacuum. The residue was subjected to chromatography on silica gel eluting with a mixture of pentane and dichloromethane (2:1, v/v) to give 3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-bromobenzene as a pale yellow oil (9.52g). A sample

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of this material (2.0g, 5.2mmol) was dissolved in anhydrous dimethylsulfoxide (30ml) and the solution was treated with potassium acetate (1.52g, 15.5mmol), bis(pinacolato)diboron (1.45g, 5.7mmol), and [1,1'-bis-(diphenylphosphino)ferroceno]-dichloropalladium (II)-dichloromethane complex (0.13g, 0.16mmol). This mixture was stirred at 80°C under an atmosphere of nitrogen for 5 hours, then cooled and then partitioned between water (100ml) and diethyl ether (4 lots of 75ml). The combined organic layers were washed twice with brine (75ml), then dried over magnesium sulfate and then concentrated under vacuum. The residue was subjected to chromatography on silica gel eluting with a mixture of pentane and dichloromethane (2:1, v/v) to give <u>B-{3-[N,N-bis-(tert-butoxycarbonyl)-aminomethyl]-phenyl}-pinacolato-boron</u> as a colorless oil (1.08g). ¹H NMR (CDCl₃, 500 MHz): δ 7.78 (s, 1H), 7.70 (m, 1H), 7.30 (m, 1H), 4.79 (s, 2H), 1.27 (s, 18H), 1.35 (s, 12H). MS(EI): 434(M⁺+H).

B. 4-{3-[N,N-Bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidine

A solution of lithium diisopropylamine (54mmol) in anhydrous tetrahydrofuran (50ml), at -78°C, was treated dropwise with a solution of benzyl 4-oxo-1-piperidinecarboxylate (11.4g, 49mmol) in anhydrous tetrahydrofuran (50ml). This mixture was stirred at -78°C for 20 minutes and then treated with a solution of N-phenyltrifluoromethanesulfonimide (19.26g, 54mmol) in anhydrous tetrahydrofuran (55ml). The resultant orange suspension was warmed to 0°C, then stirred at 0°C for 2 hours and then concentrated under vacuum. The residue was subjected to chromatography on silica gel eluting with dichloromethane to yield benzyl 1,2,3,6-tetrahydro-4-(trifluoromethylsulphonyloxy)pyridine-1-carboxylate as a yellow oil (11.34g). A portion of this material (0.84g, 2.3mmol) was dissolved in anhydrous dimethylformamide (20ml) and the solution was treated with $B-\{3-[N,N-bis-anhydrous]\}$ (tert-butoxycarbonyl)aminomethyl]-phenyl-pinacolato-boron (1.0g, 2.3mmol), potassium carbonate (0.96g, 6.7mmol) and [1,1'-bis-(diphenylphosphino)ferroceno]dichloropalladium (II)-dichloromethane complex (0.1g, 0.14mmol). This mixture was heated at 80°C under an atmosphere of nitrogen for 18 hours, then cooled and then concentrated under vacuum. The residue was partitioned between ethyl acetate (2 lots of 100ml) and water (100ml) containing concentrated ammonium hydroxide (6ml). The combined organic extracts were dried over magnesium sulfate and then concentrated under vacuum. The resultant oil was subjected to chromatography on silica gel eluting with a mixture of ethyl acetate and pentane (1:4, v/v) to yield a yellow oil (0.9g). This material was dissolved in ethanol (20ml) and the solution was treated with 10% palladium on carbon (20 mg) then stirred at ambient temperature under an atmosphere of hydrogen for 5 hours. The reaction mixture was filtered through a short pad of hyflo and the filtrate was concentrated under vacuum to give 4-{3-[N,N-bis-(tertbutoxycarbonyl)aminomethyl]-phenyl}-piperidine as colorless oil (0.54g). ¹H NMR (CDCl₃, 500 MHz): δ 7.10 (m, 4H), 4.80 (s, 2H), 4.45 (br m, 1H), 3.20 (br m, 1H), 2.98 (br m, 1H), 2.75 (br m, 1H), 1.90 (m, 1H), 1.75-1.60 (m, 3H), 1.42 (s, 18H). MS(EI): 391(M⁺+H).

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C. N,N-Bis-(tert-butoxycarbonyl)-3-[1-(5-phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine

A solution of 5-phenylethynyl-pyridine-3-carboxylic acid (0.25g, 1.1mmol) in anhydrous dimethylformamide (5ml) was treated with O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (0.42g, 1.1mmol) and diisopropylethylamine (0.5ml, 3mmol). This mixture was stirred 15 minutes at ambient temperature and then treated with a solution of 4-{3-[N,N-Bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidine (0.39g, 1.0mmol) in dimethylformamide (5ml). After stirring at ambient temperature for 18 hours the reaction mixture was concentrated under vacuum. The residue was partitioned between ethyl acetate (50ml) and saturated aqueous sodium bicarbonate (15ml). The organic layer was dried over magnesium sulfate and then concentrated under vacuum. The residue was subjected to chromatography on silica gel eluting with a mixture of dichloromethane and methanol (49:1, v/v) to give N,N-bis-(tert-butoxycarbonyl)-3-[1-(5-phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine as a yellow oil (0.25g). ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.82 (s, 1H), 8.62 (s, 1H), 8.02 (s, 1H), 7.61 (m, 2H), 7.45 (m, 3H), 7.30 (m, 1H), 7.20 (m, 1H), 7.15 (m, 1H), 7.04 (m, 1H), 4.68 (s, 2H), 4.62 (br m, 1H), 3.60 (br m, 1H), 3.23 (br m, 1H), 2.85 (m, 2H), 1.83 (br m, 1H), 1.65 (m, 3H), 1.39 (s, 18H). MS(EI): 596(M[†]+H).

D. 3-[1-(5-Phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride A solution of 3-[1-(5-phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzonitrile (0.15g, 0.25mmol) in ethyl acetate (20ml) was cooled to 0°C and then saturated with hydrogen chloride gas. The reaction mixture was stirred at ambient temperature for 4 hours and then concentrated to dryness under vacuum. The residue was treated with ethyl acetate (10ml) and the solvent removed under vacuum. This process was repeated twice to give 3-[1-(5-phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride as a white solid (0.11g). ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.83 (s, 1H), 8.63 (s, 1H), 8.08 (s, 1H), 7.61 (m, 2H), 7.45 (m, 3H), 7.44 (s, 1H), 7.37 (m, 3H), 4.64 (br m, 1H), 4.00 (m, 2H), 3.62 (br m, 1H), 3.25 (br m, 1H), 2.90 (br m, 2H), 1.88 (br m, 1H), 1.70 (m, 3H). MS(EI): 396(M⁺+H).

30 EXAMPLE 2

3-[1-(5-Phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(5-phenethyl-pyridin-3-yl)-methanone di-hydrochloride)

35 A. 5-Phenylethyl-pyridine-3-carboxylic acid

A solution of 5-phenylethynyl-pyridine-3-carboxylic acid (2g, 8.9mmol) in tetrahydrofuran (50ml) was treated with 10% palladium on carbon (200 mg) and stirred at ambient temperature under an atmosphere of hydrogen for 5 hours. The reaction mixture was filtered through a short pad of hyflo and the filtrate was concentrated under vacuum to give 5-phenylethyl-pyridine-3-carboxylic acid as white solid (2g). ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.90 (m, 1H), 8.60 (m, 1H), 8.12 (m, 1H), 7.21 (m, 5H), 3.38 (br s, 1H), 2.95 (m, 4H).

B. *N,N*-Bis-(*tert*-butoxycarbonyl)-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine

By proceeding in a similar manner to the method described in EXAMPLE 1C, but using of 5-phenylethyl-pyridine-3-carboxylic acid, there was prepared N,N-bis-(tert-butoxycarbonyl)-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine as a white amorphous solid. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.50 (s, 1H), 8.41 (s, 1H), 7.61 (m, 1H), 7.30-7.05 (m, 9H), 4.68 (s, 2H), 4.62 (br m, 1H), 3.48 (br m, 1H), 3.35 (s, 4H), 3.18 (br m, 1H), 2.85 (m, 2H), 1.82 (br m, 1H), 1.65 (br m, 1H), 1.58 (br m, 2H), 1.39 (s, 18H). MS(EI): 600(M⁺+H).

C. 3-[1-(5-Phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 1D, but using *N*,*N*-bis-(*tert*-butoxycarbonyl)-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine in place of *N*,*N*-Bis-(tert-butoxycarbonyl)-3-[1-(5-phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine, there was prepared 3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride as a white solid. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.90 (m, 2H), 8.42 (s, 1H), 7.58 (m, 1H), 7.38-7.20 (m, 8H), 4.62 (br m, 1H), 4.00 (m, 2H), 3.45 (br m, 1H), 3.20 (br m, 1H), 3.17 (m, 2H), 3.00 (m, 2H), 2.90 (br m, 2H), 1.88 (br m, 1H), 1.70 (br m, 3H). MS(EI): 400(M⁺+H).

EXAMPLE 3

3-[1-(1-oxy-5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine hydrochloride

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(1-oxy-5-phenethyl-pyridin-3-yl)-methanone hydrochloride)

A solution of *N*,*N*-Bis-(*tert*-butoxycarbonyl)-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine (100mg, 0.17mmol, EXAMPLE 2B) in dichloromethane (10ml) was treated with meta-chloroperbenzoic acid (80%, 80mg, 0.37mmol). After stirring for 18 hours at ambient temperature the reaction mixture was diluted with dichloromethane (40ml) and then washed three times with saturated

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aqueous sodium bicarbonate solution (20ml). The organic phase was dried over magnesium sulfate and then concentrated under vacuum. The residue was subjected to chromatography on silica gel eluting with a mixture of dichloromethane and methanol (98:2, v/v) to give *N,N*-bis-(*tert*-butoxycarbonyl)-3-[1-(1-oxy-5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine as a colorless oil (70mg). This material was dissolved in ethyl acetate (10ml) and the solution was cooled to 0°C, then saturated with hydrogen chloride gas, then stirred at ambient temperature for 4 hours and then concentrated to dryness under vacuum. The residue was treated with ethyl acetate (10ml) and the solvent removed under vacuum. This process was repeated twice to leave the title compound as a white solid (45mg). ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.39 (s, 1H), 8.30 (s, 1H), 7.45 (s, 1H), 7.40 (s, 1H), 7.38-7.18 (m, 8H), 4.59 (br m, 1H), 4.00 (m, 2H), 3.50 (br m, 1H), 3.20 (br m, 1H), 2.98 (s, 4H), 2.85 (br m, 2H), 1.84 (br m, 1H), 1.68 (br m, 3H). MS(EI): 416(M⁺+H).

EXAMPLE 4

3-[1-(Quinoline-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-quinolin-3-yl-methanone di-hydrochloride)
By proceeding in a similar manner to the method described in EXAMPLE 1, but using quinoline-3-carboxylic acid in place of 5-phenylethynyl-pyridine-3-carboxylic acid, there was prepared the <u>title compound</u> as a white amorphous solid. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 9.10 (s, 1H), 8.78 (s, 1H), 8.20 (m, 2H), 7.98 (m, 1H), 7.80 (m, 1H), 7.50 (s, 1H), 7.35 (m, 3H), 4.72 (br m, 1H), 4.00 (m, 2H), 3.80 (br m, 1H), 3.30 (br m, 1H), 2.90 (br m, 2H), 1.90 (br m, 1H), 1.75 (br m, 3H). MS(EI): 346(M⁺+H).

EXAMPLE 5

3-[1-(3-Phenylethynyl-benzoyl)-piperidin-4-yl]-benzylamine hydrochloride

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(3-phenylethynyl-phenyl)-methanone hydrochloride)

A. N,N-Bis-(tert-butoxycarbonyl)-3-[1-(3-ethynyl-benzoyl)-piperidin-4-yl]-benzylamine
By proceeding in a similar manner to the method described in EXAMPLE 1C, but using of 3-ethynyl-benzoic acid [prepared according to the procedure described by C. Eaborn et al., J. Chem. Soc. C, 1967, (15), pages 1364-1366] in place of 5-phenylethynyl-pyridine-3-carboxylic acid, there was prepared N,N-bis-(tert-butoxycarbonyl)-3-[1-(3-ethynyl-benzoyl)-piperidin-4-yl]-benzylamine as a white amorphous solid. ¹H NMR (CDCl₃, 500 MHz): δ 7.76 (m, 2H), 7.40 (m, 2H), 7.25 (m, 2H), 7.10 (m, 4H), 4.95 (br m, 1H), 4.79 (s, 2H), 3.80 (br m, 1H), 3.10 (br m, 1H), 2.84 (br m, 1H), 2.78 (br m, 1H), 1.90 (m, 1H), 1.75 (m, 3H), 1.42 (s, 18H). MS(EI): 541(M+Na).

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B. N.N-Bis-(tert-butoxycarbonyl)-3-[1-(3-phenylethynyl-benzoyl)-piperidin-4-yl]-benzylamine
A mixture of N,N-bis-(tert-butoxycarbonyl)-3-[1-(3-ethynyl-benzoyl)-piperidin-4-yl]-benzylamine
(0.24g, 0.46mmol), iodobenzene (95mg, 0.46mmol), dichlorobis(triphenylphosphine)palladium (II)
(35mg, 0.05mmol), copper (I) iodide (26mg, 0.14mmol), triethylamine (0.57ml, 4.1mmol) and
anhydrous dimethylformamide (8ml) was stirred at ambient temperature under nitrogen for 18 hours.
The solvent was removed under vacuum and the residue was partitioned between ethyl acetate (3 lots
of 50ml) and water (20ml). The combined organic layers were washed with brine (50ml), then dried
over magnesium sulfate and then concentrated under vacuum. The residue was subjected to
chromatography on silica gel eluting with a mixture of cyclohexane and ethyl acetate (3:2, v/v) to give
N,N-bis-(tert-butoxycarbonyl)-3-[1-(3-phenylethynyl-benzoyl)-piperidin-4-yl]-benzylamine as a
yellow oil (0.23g). ¹H NMR (CDCl₃, 500 MHz): δ 7.58 (m, 4H), 7.40 (m, 5H), 7.25 (m, 1H), 7.10
(m, 3H), 4.90 (br m, 1H), 4.79 (s, 2H), 3.80 (br m, 1H), 3.15 (br m, 1H), 2.84 (br m, 1H), 2.78 (br m,
1H), 1.95 (m, 1H), 1.80 (m, 3H), 1.42 (s, 18H). MS(EI): 617(M⁺+ Na).

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C. 3-[1-(3-Phenylethynyl-benzoyl)-piperidin-4-yl]-benzylamine hydrochloride

A solution of *N*,*N*-Bis-(*tert*-butoxycarbonyl)-3-[1-(3-phenylethynyl-benzoyl)-piperidin-4-yl]-benzylamine (100mg, 0.17mmol) in methanol (10ml), cooled to 0 °C, was saturated with hydrogen chloride gas. The mixture was stirred at ambient temperature for 4 hours then concentrated to dryness under vacuum. The residue was triturated with a mixture of dichloromethane and diethyl ether to give 3-[1-(3-phenylethynyl-benzoyl)-piperidin-4-yl]-benzylamine hydrochloride as a white amorphous solid (46mg). ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 7.61-7.30 (m, 13H), 4.62 (br m, 1H), 4.00 (s, 2H), 3.62 (br m, 1H), 3.25 (br m, 1H), 2.85 (br m, 2H), 1.88 (br m, 1H), 1.70 (br m, 3H). MS(EI): 395(M⁺+H).

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EXAMPLE 6

2-{3-[4-(3-Aminomethyl-phenyl)-piperidine-1-carbonyl]-phenyl}-1-(4-hydroxyphenyl)-ethanone (A.K.A. 2-{3-[4-(3-Aminomethyl-phenyl)-piperidine-1-carbonyl]-phenyl}-1-(4-hydroxy-phenyl)-ethanone hydrochloride)

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A. N,N-Bis-(tert-butoxycarbonyl)-3-{1-[3-(4-hydroxyphenyl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine

By proceeding in a similar manner to the method described in EXAMPLE 5B, but using 4-iodophenol in place of iodobenzene, there was prepared N,N-bis-(tert-butoxycarbonyl)-3-{1-[3-(4-

35 hydroxyphenyl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine as a yellow amorphous solid. ¹H NMR

(CDCl₃, 500 MHz): δ 7.58 (m, 2H), 7.40 (m, 4H), 7.25 (m, 1H), 7.15 (m, 3H), 6.80 (m, 2H), 4.90 (br m, 1H), 4.79 (s, 2H), 3.90 (br m, 1H), 3.15 (br m, 1H), 2.84 (br m, 1H), 2.78 (br m, 1H), 1.98 (m, 1H), 1.80 (m, 3H), 1.42 (s, 18H). MS(EI): 633(M⁺+ Na).

5 B. 2-{3-[4-(3-Aminomethyl-phenyl)-piperidine-1-carbonyl]-phenyl}-1-(4-hydroxyphenyl)-ethanone hydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 5C but using *N*,*N*-bis-(*tert*-butoxycarbonyl)-3-{1-[3-(4-hydroxyphenyl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine, there was prepared 2-{3-[4-(3-aminomethyl-phenyl)-piperidine-1-carbonyl]-phenyl}-1-(4-hydroxyphenyl)-

ethanone hydrochloride as a white amorphous solid. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 7.92 (m, 2H), 7.40-7.28 (m, 8H), 6.82 (m, 2H), 4.60 (br m, 1H), 4.38 (s, 2H), 4.00 (s, 2H), 3.62 (br m, 1H), 3.18 (br m, 1H), 2.80 (br m, 2H), 1.88 (br m, 1H), 1.70-1.60 (br m, 3H), MS(EI): 429(M⁺+H).

EXAMPLE 7

3-{1-[3-(6-Amino-pyridin-3-yl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine hydrochloride (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-[3-(6-amino-pyridin-3-ylethynyl)-phenyl]-methanone hydrochloride)

A. 3-Iodo-6-(tert-butoxycarbonylamino)pyridine

A stirred solution of 6-amino-3-iodopyridine (0.44g, 2.0mmol) in anhydrous tetrahydrofuran (7ml), under nitrogen, was treated dropwise with a solution of sodium bis(trimethylsilyl)amide (1M, 4.4ml, 4.4mmol). After stirring for a further 15 minutes the mixture was treated with a solution of di-*tert*-butyldicarboxylate (440 mg, 2mmol) in anhydrous tetrahydrofuran (3ml). The resulting thick slurry was stirred at ambient temperature for 18 hours then partitioned between ethyl acetate (3 lots of 50ml) and water (50ml). The combined organics were dried over sodium sulfate then concentrated under vacuum. The residue was subjected to chromatography on silica gel eluting with a mixture of cyclohexane and ethyl acetate (9:1, v/v) to give 3-iodo-6-(*tert*-butoxycarbonylamino)pyridine as a white solid (0.56g). ¹H NMR (CDCl₃, 500MHz) δ8.50 (s, 1H), 7.92 (m, 1H), 7.85 (m, 1H), 1.58 (s, 9H). MS(EI): 319(M⁺- H).

B. *N*,*N*-Bis-(*tert*-butoxycarbonyl)-3-{1-[3-(6-*tert*-butoxycarbonylamino-pyridin-3-yl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine

By proceeding in a similar manner to the method described in EXAMPLE 5B, but using 3-iodo-6-(tert-butoxycarbonylamino)pyridine in place of iodobenzene, there was prepared <u>N,N-bis-(tert-</u>

butoxycarbonyl)-3-{1-[3-(6-tert-butoxycarbonylamino-pyridin-3-yl)ethynyl-benzoyl]-piperidin-4-yl}-

benzylamine as a yellow amorphous solid. ¹H NMR (CDCl₃, 500MHz): δ 8.41 (s, 1H), 7.99 (m, 1H), 7.80 (m, 1H), 7.61 (s, 1H), 7.59 (m, 2H), 7.40 (m, 2H), 7.23 (m, 1H), 7.12 (m, 3H), 4.90 (br m, 1H), 4.79 (s, 2H), 3.84 (br m, 1H), 3.15 (br m, 1H), 2.84 (br m, 1H), 2.78 (br m, 1H), 1.95 (m, 1H), 1.80 (m, 3H), 1.55 (s, 9H), 1.42 (s, 18H). MS(EI): 710(M⁺).

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C. 3-{1-[3-(6-Amino-pyridin-3-yl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine hydrochloride By proceeding in a similar manner to the method described in EXAMPLE 5C but using *N,N*-bis-(*tert*-butoxycarbonyl)-3-{1-[3-(6-*tert*-butoxycarbonylamino -pyridin-3-yl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine, there was prepared 3-{1-[3-(6-Amino-pyridin-3-yl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine hydrochloride as a white amorphous solid.). ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.22 (s, 1H), 8.15 (br s, 2H), 7.90 (m, 1H), 7.60-7.41 (m, 5H), 7.30 (m, 3H), 6.93 (m, 1H), 4.60 (br m, 1H), 4.00 (m, 2H), 3.62 (br m, 1H), 3.25 (br m, 1H), 2.85 (br m, 2H), 1.84 (br m, 1H), 1.60 (br m, 3H). MS(EI): 411(M⁺+H).

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EXAMPLE 8

3-{1-[3-(4-hydroxymethylphenyl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine hydrochloride (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-[3-(4-hydroxymethyl-phenylethynyl)-phenyl]-methanone hydrochloride)

By proceeding in a similar manner to the method described in EXAMPLE 5, but using 4-iodobenzylalcohol (prepared according to the procedure described by D.S.Tan et al., J. Am. Chem. Soc., 1998, 120(33), pages 8565-8566) in place of iodobenzene, there was prepared the <u>title compound</u> as a white amorphous solid. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 7.61-7.25 (m, 12H), 5.33 (m, 1H), 4.62 (br m, 1H), 4.58 (m, 2H), 4.00 (s, 2H), 3.62 (br m, 1H), 3.20 (br m, 1H), 2.83 (br m, 2H), 1.84 (br m, 1H), 1.72-1.62 (br m, 3H). MS(EI): 425(M⁺+H).

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EXAMPLE 9

3-[1-(3-Phenylethyl-benzoyl)-piperidin-4-yl]-benzylamine hydrochloride

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(3-phenethyl-phenyl)-methanone hydrochloride) A solution of N,N-bis-(tert-butoxycarbonyl)-3-[1-(3-phenylethynyl-benzoyl)-piperidin-4-yl]-benzylamine (110mg, 0.18mmol, EXAMPLE 5B) in ethanol (10ml) was treated with 10% palladium on carbon (20mg) and then stirred at ambient temperature under an atmosphere of hydrogen for 8 hours. The reaction mixture was filtered through a short pad of hyflo and then concentrated under vacuum to give a white amorphous solid (0.54g). This material was treated with methanolic hydrogen chloride according to the procedure described in EXAMPLE 5C to give the title compound as white amorphous solid (25mg). ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 7.40-7.15 (m, 13H), 4.62 (br m, 1H),

4.00 (s, 2H), 3.60 (br m, 1H), 3.10 (br m, 1H), 2.80 (br m, 2H), 1.85 (br m, 1H), 1.60 (br m, 3H), MS(EI): 399(M⁺+H).

EXAMPLE 10

3-{1-[3-(4-hydroxyphenyl)ethyl-benzoyl]-piperidin-4-yl}-benzylamine hydrochloride
(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-{3-[2-(4-hydroxy-phenyl)-ethyl]-phenyl}methanone hydrochloride)
By proceeding in a similar manner to the method described in EXAMPLE 9, but using N,N-bis-(tert-butoxycarbonyl)-3-{1-[3-(4-hydroxyphenyl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine
(EXAMPLE 6A), there was prepared the title compound as a white amorphous solid. ¹H NMR
[(CD₃)₂SO, 500 MHz]: δ 9.18 (br s, 1H), 7.41 (s, 1H), 7.35 (m, 5H), 7.20 (m, 2H), 6.98 (m, 2H), 6.60 (m, 2H), 4.82 (br m, 1H), 4.00 (m, 2H), 3.80 (br m, 1H), 3.10 (br m, 1H), 2.80 (m, 6H), 1.82 (br m, 1H), 1.70 (br m, 1H), 1.60 (br m, 2H). MS(EI): 415(M⁺+ H).

EXAMPLE 11

3-{1-[3-(6-amino-pyridin-3-yl)ethyl-benzoyl]-piperidin-4-yl}-benzylamine hydrochloride (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-{3-[2-(6-amino-pyridin-3-yl)-ethyl]-phenyl}-methanone hydrochloride)

By proceeding in a similar manner to the method described in EXAMPLE 9, but using N,N-bis-(tert-butoxycarbonyl)-3-{1-[3-(6-tert-butoxycarbonylamino-pyridin-3-yl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine (EXAMPLE 7B), there was prepared the <u>title compound</u> as a white amorphous solid. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 7.90 (br s, 2H), 7.85 (m, 1H), 7.76 (s, 1H), 7.43 (s, 1H), 7.40-7.30 (m, 5H), 7.24 (m, 2H), 6.93 (m, 1H), 4.61 (br m, 1H), 4.00 (m, 2H), 3.60 (br m, 1H), 3.15 (br m, 1H), 2.92 (br m, 6H), 1.90 (br m, 1H), 1.70 (br m, 1H), 1.60 (br m, 2H). MS(EI): 415(M⁺+H).

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EXAMPLE 12

3-[1-(4-Phenylethyl-thiophene-2-carbonyl)-piperidin-4-yl]-benzylamine hydrochloride (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(4-phenethyl-thiophen-2-yl)-methanone hydrochloride)

By proceeding in a similar manner to the method described in EXAMPLE 1, but using 4-phenylethylthiophene-2-carboxylic acid (prepared according the procedure described by S.Gronowitz et al.,
Heterocycles, 1981, 15(2), pages 947-959) in place of 5-phenylethynyl-pyridine-3-carboxylic acid,
there was prepared the <u>title compound</u> as a white amorphous solid. ¹H NMR [(CD₃)₂SO, 500 MHz]:
δ 7.41-7.18 (m, 11H), 4.37 (br m, 1H), 4.00 (m, 2H), 3.05 (br m, 2H), 2.98 (s, 4H), 2.85 (br m, 2H),
1.90 (br m, 2H), 1.60 (br m, 2H), MS(EI): 405(M⁺+H).

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EXAMPLE 13

3-[1-(5-Phenylethyl-thiophene-2-carbonyl)-piperidin-4-yl]-benzylamine hydrochloride (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(5-phenethyl-thiophen-2-yl)-methanone hydrochloride)

By proceeding in a similar manner to the method described in EXAMPLE 2, but using 5-phenylethynyl-thiophene-2-carboxylic acid in place of 5-phenylethynyl-pyridine-3-carboxylic acid, there was prepared the <u>title compound</u> as a white amorphous solid. 1 H NMR [(CD₃)₂SO, 500 MHz]: δ 7.41 (s, 1H), 7.38-7.20 (m, 9H), 6.83 (s, 1H), 4.40 (br m, 1H), 4.00 (br s, 2H), 3.12 (m, 2H), 3.08 (br m, 2H), 2.98 (m, 2H), 2.85 (br m, 2H), 1.82 (br m, 2H), 1.60 (br m, 2H), MS(EI): 405(M⁺+H).

EXAMPLE 14

3-{1-[3-(Benzooxazo-2-yl)-benzoyl]-piperidin-4-yl}-benzylamine hydrochloride
(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(3-benzoxazol-2-yl-phenyl)-methanone hydrochloride)

By proceeding in a similar manner to the method described in EXAMPLE 1, but using 3-(benzooxazo-2-yl)-benzoic acid (prepared according to the procedure described by V.F.Bystrov et al., Zh. Obshch. Khim., 1968, 38(5), pages 1001-1005) in place of 5-phenylethynyl-pyridine-3-carboxylic acid, there was prepared the <u>title compound</u> as a white amorphous solid. 1 H NMR [(CD₃)₂SO, 500 MHz]: δ 8.28 (m, 1H), 8.19 (s, 1H), 7.81 (m, 2H), 7.50 (m, $\dot{2}$ H), 7.43 (m, 3H), 7.30 (m, 3H), 4.66 (br m, 1H), 4.00 (m, 2H), 3.70 (br m, 1H), 3.25 (br m, 1H), 2.92 (br m, 1H), 2.82 (br m, 1H), 1.90 (br m, 1H), 1.70 (br m, 3H), MS(EI): $412(M^{+}+H)$.

EXAMPLE 15

- 25 3-[1-(3-Phenoxymethyl-benzoyl)-piperidin-4-yl]-benzylamine hydrochloride
 (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(3-phenoxymethyl-phenyl)-methanone hydrochloride)
 - By proceeding in a similar manner to the method described in EXAMPLE 1, but using 3-phenoxymethyl-benzoic acid (prepared according to the procedure of H.Oelschlaeger et al., Arch.
- Pharm. (Weinheim, Ger.), 1978, 311(2), pages 81-97) in place of 5-phenylethynyl-pyridine-3-carboxylic acid, there was prepared the title compound as a white amorphous solid. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 7.58-7.25 (m, 10H), 7.00 (m, 2H), 6.96 (m, 1H), 5.18 (s, 2H), 4.62 (br m, 1H), 4.00 (m, 2H), 3.62 (br m, 1H), 3.18 (br m, 1H), 2.82 (br m, 2H), 1.88 (br m, 1H), 1.65 (br m, 3H), MS(EI): 401(M⁺+H).

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EXAMPLE 16

3-{1-[3-(2-E-Phenylethenyl)-benzoyl]-piperidin-4-yl}-benzylamine hydrochloride

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-[3-((E)-styryl)-phenyl]-methanone hydrochloride)

By proceeding in a similar manner to the method described in EXAMPLE 1, but using 3-(2-E-phenylethenyl)-benzoic acid (prepared according to the procedure of N.A.Bumagin et al., Zh. Org.

Khim., 1995, 31(4), pages481-487) in place of 5-phenylethynyl-pyridine-3-carboxylic acid, there was prepared the title compound as a white amorphous solid. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 7.71

(m, 1H), 7.63 (m, 3H), 7.50 (m, 2H), 7.40-7.25 (m, 9H), 4.63 (br m, 1H), 4.00 (s, 2H), 3.71 (br m, 1H), 3.10 (br m, 1H), 2.84 (br m, 2H), 1.88 (br m, 1H), 1.70 (br m, 3H), MS(EI): 397(M⁺+H).

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EXAMPLE 17

4-Fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride (A.K.A. [4-(5-Aminomethyl-2-fluoro-phenyl)-piperidin-1-yl]-(5-phenethyl-pyridin-3-yl)-methanone di-hydrochloride)

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A. 4-(Pinacolatoboronyl)-1,2,3,6-tetrahydro-pyridine trifluoroacetate

A solution of lithium diisopropylamine (59mmol) in anhydrous tetrahydrofuran (50ml) at -78°C was treated dropwise with a solution of tert-butyl 4-oxo-1-piperidinecarboxylate (10.7g, 54mmol) in anhydrous tetrahydrofuran (70ml). After stirring at -78°C for a further 20 minutes the reaction mixture was treated with a solution of N-phenyltrifluoromethanesulfonimide (21.2g, 59mmol) in anhydrous tetrahydrofuran (90ml). The resultant orange suspension was warmed to 0°C, then stirred at 0°C for 3 hours and then concentrated under vacuum. The residue was subjected to chromatography on silica gel eluting with a mixture of pentane and dichloromethane (1:1, v/v) and then subjected to chromatography on alumina eluting with a mixture of pentane and ethyl acetate (9:1, v/v) to yield tertbutyl 1,2,3,6-tetrahydro-4-(trifluoromethylsulphonyloxy)-pyridine-1-carboxylate as a yellow oil (15g). A portion of this material (1.72g, 5.2mmol) was dissolved in anhydrous dioxane (30ml) and the solution was treated with bis(pinacolato)diboron (1.46g, 5.75mmol), potassium acetate (1.54g, 15.7mmol), (diphenylphosphino)-ferrocene (86mg, 0.16mmol) and [1,1'-bis-(diphenylphosphino)ferroceno]-dichloropalladium (II) (114mg, 0.16mmol). The reaction mixture was heated at 80°C under an atmosphere of nitrogen for 18 hours, then cooled and then concentrated under vacuum. The residue was partitioned between ethyl acetate (2 lots of 100ml) and water (100ml). The combined organic extracts were dried over magnesium sulfate then concentrated under vacuum. The resultant oil was subjected to chromatography on silica gel eluting with a mixture of ethyl acetate and pentane (1:8, v/v) to yield a yellow oil (1.4g). A solution of this material in dichloromethane (10ml), cooled to 0°C, was treated with trifluoracetic acid (3.9ml). The mixture was stirred at ambient temperature for 2 hours then concentrated under vacuum to leave 4-(pinacolatoboronyl)-1,2,3,6--

tetrahydro-pyridine trifluoroacetate as a brown oil. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.76 (br s, 2H), 6.39 (br s, 1H), 3.61 (br m, 2H), 3.11 (br m, 2H), 2.23 (br m, 2H), 1.20 (s 12H). MS(EI): 210(M⁺+ H).

B. 1-(5-Phenylethyl-pyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6-tetrahydro-pyridine 5 A solution of 5-phenylethyl-pyridine-3-carboxylic acid (0.46g, 2.0mmol, EXAMPLE 2A) in anhydrous dimethylformamide (9ml) was treated with O-(7-azabenzotriazol-1-yl)-1,1,3,3tetramethyluronium hexafluorophosphate (0.87g, 2.2mmol) and diisopropylethylamine (1.7ml, 10mmol). This mixture was stirred at ambient temperature for 10 minutes then treated with a solution 10 of 4-(pinacolatoboronyl)-1,2,3,6-tetrahydro-pyridine trifluoroacetate (0.81g, 2.5mmol) in dimethylformamide (9ml). The reaction mixture was stirred at ambient temperature for 18 hours and then concentrated under vacuum. The residue was partitioned between dichloromethane (2 lots of 50ml) and saturated aqueous sodium bicarbonate (15ml). The combined organic layers were dried over magnesium sulfate and then concentrated under vacuum. The residue was subjected to 15 chromatography on silica gel eluting with ethyl acetate to give 1-(5-phenylethyl-pyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6-tetrahydro-pyridine as a brown amorphous solid (0.73g). 1H NMR [(CD₃)₂SO, 500 MHz]: δ 8.49 (s, 1H), 8.40 (s, 1H), 7.61 (s, 1H), 7.20 (m, 5H), 6.48 (br s, 1H), 4.18 (br m, 1H), 3.83 (br m, 1H), 3.62 (br m, 1H), 3.23 (br m, 1H), 2.98 (m, 4H), 2.17 (br m, 2H), 1.20 (s, 12H). MS(EI): 441(M++Na).

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C. N-(tert-Butoxycarbonyl)-3-bromo-4-fluoro-benzylamine

A mixture of 3-bromo-4 fluoro-benzylamine hydrochloride (2.41g, 10mmol), triethylamine (2.8ml, 20mmol), and di-*tert*-butoxycarbonate (1.8g, 10.3mmol) in dichloromethane (20ml) was stirred at ambient temperature for 18 hours then washed with water (20ml). The organic phase was dried over magnesium sulfate and then concentrated under vacuum. The residue was subjected to chromatography on silica gel eluting with a mixture of cyclohexane and ethyl acetate (3:1, v/v) to give N-(*tert*-butoxycarbonyl)-3-bromo-4-fluoro-benzylamine as a white solid (1.4g). ¹H NMR (CDCl₃, 500 MHz): δ 7.45 (m, 1H), 7.20 (m, 1H), 7.08 (m, 1H), 4.85 (br s, 1H), 4.21 (m, 2H), 1.42 (s, 9H).

30 <u>D. N-(tert-Butoxycarbonyl)-4-fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-1,2,3,6-tetrahydro-pyridin-4-yl]-benzylamine</u>

A mixture of N-(*tert*-butoxycarbonyl)-3-bromo-4-fluoro-benzylamine (0.28g, 0.92mmol), anhydrous dimethylformamide (10ml), 1-(5-phenylethyl-pyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6-tetrahydro-pyridine (0.37g, 0.88mmol), potassium carbonate (0.36g, 2.6mmol) and [1,1'-bis-(diphenylphosphino)ferrocenoldichloropalladium (II)-dichloromethane complex (43 mg, 0.05mmol)

was heated at 80°C under an atmosphere of nitrogen for 18 hours. The reaction mixture was cooled to room temperature and then concentrated under vacuum. The residue was partitioned between ethyl acetate (2 lots of 50ml) and water (10ml). The combined organic extracts were dried over magnesium sulfate and then concentrated under vacuum. The resultant oil was subjected to chromatography on silica gel eluting with ethyl acetate to yield N-(tert-butoxycarbonyl)-4-fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-1,2,3,6-tetrahydro-pyridin-4-yl]-benzylamine as a pale yellow oil (0.18g). ¹H NMR (CDCl₃, 500 MHz): δ 8.58 (s, 1H), 8.50 (s, 1H), 7.51 (s, 1H), 7.25 (m, 2H), 7.18 (m, 5H), 7.00 (m, 1H), 6.01 (br s, 1H), 4.83 (br s, 1H), 4.38 (br m, 1H), 4.27 (m, 2H), 3.98 (br m, 2H), 3.50 (br m, 1H), 2.99 (m, 4H), 2.60 (br m, 1H), 2.50 (br m, 1H). MS(EI): 538(M⁺+ Na).

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E. 4-Fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride A solution of *N*-(*tert*-butoxycarbonyl)-4-fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-1,2,3,6-tetrahydro-pyridin-4-yl]-benzylamine in ethanol (12ml) was treated with 10% palladium on carbon (75mg) and the mixture was stirred at ambient temperature under an atmosphere of hydrogen for 72 hours. The reaction mixture was filtered through a short pad of hyflo and the filtrate was concentrated under vacuum to give *N*-(*tert*-butoxycarbonyl-4-fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine as colorless oil (85mg). This material was dissolved in methanol (10ml) and the solution was cooled to 0°C and then saturated with hydrogen chloride gas. This mixture was stirred at ambient temperature for 4 hours and then concentrated to dryness under vacuum. The residue was triturated with a mixture of dichloromethane and diethyl ether to give 4-fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride as a white amorphous solid (50mg). ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.60 (s, 1H), 8.58 (s, 1H), 7.83 (s, 1H), 7.60 (m, 1H), 7.38 (m, 1H), 7.20 (m, 6H), 4.61 (br m, 1H), 4.00 (m, 2H), 3.50 (br m, 1H), 3.20 (br m, 2H), 2.99 (m, 2H), 2.95 (m, 2H), 2.90 (br m, 1H), 1.82 (br m, 1H), 1.65 (br m, 3H). MS(EI): 418(M⁺+H).

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EXAMPLE 18

4-Methyl-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride (A.K.A. [4-(5-Aminomethyl-2-methyl-phenyl)-piperidin-1-yl]-(5-phenethyl-pyridin-3-yl)-methanone di-hydrochloride)

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A. 4-[N,N-Bis-(tert-butoxycarbonyl)aminomethyl]-2-bromo-toluene

A solution of 4-methyl-3-bromobenzylbromide (1.63g, 6.2mmol, prepared according to the procedure described in International Patent Application No. WO 0009475) and di-tert-butyliminodicarboxylate (1.48g, 6.8mmol) in anhydrous tetrahydrofuran (15ml) was treated portionwise with sodium hydride (0.27g of 60% dispersion in mineral oil, 6.8mmol). The mixture was stirred at ambient temperature for

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18 hours then partitioned between saturated aqueous ammonium chloride solution (20ml) and ethyl acetate (3 lots of 80ml). The combined organic layers were washed with brine (80ml), then dried over magnesium sulfate and concentrated under vacuum. The residue was subjected to chromatography on silica gel eluting with a mixture of cyclohexane and diethyl ether (9:1, v/v) to give 4-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-2-bromo-toluene as a pale yellow oil (2.4g). ¹H NMR (CDCl₃, 500 MHz): δ 7.45 (s, 1H), 7.18 (m, 2H), 4.71 (s, 2H), 2.38 (s, 3H), 1.43 (s, 18H).

B. 4-Methyl-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride By proceeding in a similar manner to the method described in EXAMPLE 17, but using 4-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-2-bromo-toluene in place of N-(tert-butoxycarbonyl)-3-bromo-4-fluoro-benzylamine, there was prepared 4-methyl-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride as a white amorphous solid. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.60 (m, 2H), 7.83 (s, 1H), 7.41 (s, 1H), 7.20 (m, 7H), 4.62 (br m, 1H), 3.98 (m, 2H), 3.45 (br m, 1H), 3.20 (br m, 1H), 3.07 (m, 2H), 3.00 (m, 2H), 2.95 (m, 2H), 2.32 (s, 3H), 1.80 (br m, 1H), 1.70 (br m, 3H). MS(EI): 414(M⁺+H).

EXAMPLE 19

3-{1-[3-(5-Phenyl-1,3,4-oxadiazol-2-yl)-phenylcarbonyl]-piperidin-4-yl}-benzylamine hydrochloride (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-[3-(5-phenyl-1,3,4-oxadiazol-2-yl)-phenyl]-methanone hydrochloride)

A. 3-(5-Phenyl-1,3,4-oxadiazol-2-yl)-benzoic acid

A mixture of methyl hydrogen isopthalalate (1.8g, 10mmol), benzoic hydrazide (1.4g, 10mmol) and phosphorous oxychloride (20ml), under an atmosphere of nitrogen, was heated at 120°C for 18 hours, then cooled to room temperature and then poured into ice water (500ml). This mixture was treated with solid sodium carbonate until the aqueous layer was basic (pH 8 -9) and the resultant pink solid was filtered. This material was treated with 100ml methanol and the suspension was treated with sodium hydroxide solution (30ml, 1M). The reaction mixture was heated at reflux for 4 hours, then cooled and then concentrated to dryness. The residue was dissolved in water (100ml) and the solution was acidified to pH 3 by addition of concentrated hydrochloric acid. The resultant precipitate was filtered, then dried and then subjected to chromatography on silica gel eluting with a mixture of dichloromethane and methanol (98:2, v/v) to yield 3-(5-phenyl-1,3,4-oxadiazol-2-yl)-benzoic acid as a white solid (600mg). ¹H NMR [(CD₃)₂SO, 500 MHz]: 8 8.80 (s, 1H), 8.38 (m, 1H), 8.18 (m, 3H), 7.78 (m, 1H), 7.62 (m, 3H). MS(EI): 265(M⁺- H).

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B. 3-{1-[3-(5-Phenyl-1,3,4-oxadiazol-2-yl)-phenylcarbonyl]-piperidin-4-yl}-benzylamine hydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 1, but using 3-(5-phenyl-1,3,4-oxadiazol-2-yl)-benzoic acid in place of 5-phenylethynyl-pyridine-3-carboxylic acid, there was prepared 3-{1-[3-(5-phenyl-1,3,4-oxadiazol-2-yl)-phenylcarbonyl]-piperidin-4-yl}-benzylamine hydrochloride as a pale yellow amorphous solid. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.21 (m, 1H), 8.20 (m, 3H), 7.75 (m, 2H), 7.68 (m, 3H), 7.50 (s, 1H), 7.37 (m, 3H), 4.70 (br m, 1H), 4.00 (m, 2H), 3.70 (br m, 1H), 3.25 (br m, 1H), 2.90 (br m, 1H), 2.85 (br m, 1H), 1.88 (br m, 1H), 1.70 (m, 3H), MS(EI): 439(M⁺+H).

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EXAMPLE 20

3-[1-(Indole-6-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(1H-indol-6-yl)-methanone trifluoroacetate) A solution of diisopropylamine in dimethylformamide (1ml, 180μM) in a glass vial was treated with a solution of O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate in dimethylformamide (1ml, 60μM) followed by a solution of indole-6-carboxylic acid in dimethylformamide (1ml, 60μM). After standing at ambient temperature for 15 minutes the mixture was treated with a solution of 4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidine in dimethylformamide(1ml, 60μM, EXAMPLE 1B). The reaction mixture was allowed to stand at ambient temperature for 18 hours then evaporated. The residue was treated with chloroform (5ml) and aqueous sodium carbonate solution (5%). This mixture was shaken gently for 30 minutes, poured into a fritted polypropylene tube and the organic layer which passes through the frit collected in a glass vial. The chloroform was evaporated under vacuum and the residue was treated with a mixture of trifluoroacetic acid, dichloromethane and water (4ml, 55/40/5, v/v/v). This mixture was shaken gently for 2 hours and then evaporated to leave the title compound as a yellow oil. LC-MS: R_T = 3.43 minutes (>96% by ELSD); MS (ES⁺), 334 (MH⁺).

EXAMPLE 21

3-[1-(Coumarin-3-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate

30 (A.K.A. 3-[4-(3-Aminomethyl-phenyl)-piperidine-1-carbonyl]-1-benzopyran-2-one trifluoroacetate)
By proceeding in a similar manner to the method described in EXAMPLE 20, but using coumarin-3carboxylic acid in place of indole-6-carboxylic acid, there was prepared the <u>title compound</u> as a yellow
oil. LC-MS: R_T = 3.15 minutes (>86% by ELSD); MS (ES⁺), 363 (MH⁺).

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3-[1-(Naphthyl-2-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-naphthalen-2-yl-methanone trifluoroacetate) By proceeding in a similar manner to the method described in EXAMPLE 20, but using 2-naphthoic acid in place of indole-6-carboxylic acid, there was prepared the <u>title compound</u> as a yellow oil. LC-

5 MS: $R_T = 3.66$ minutes (100% by ELSD); MS (ES⁺), 345 (MH⁺).

EXAMPLE 23

3-{1-[3-(2-Naphthylthio)propionyl]-piperidin-4-yl}-benzylamine trifluoroacetate (A.K.A. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-(naphthalen-2-ylsulfanyl)-propan-1-one

10 trifluoroacetate)

By proceeding in a similar manner to the method described in EXAMPLE 20, but using 3-(2-naphthylthio)propionic acid in place of indole-6-carboxylic acid, there was prepared the <u>title</u> compound as a yellow oil. LC-MS: $R_T = 4.00$ minutes (>95% by ELSD); MS (ES⁺), 405(MH⁺).

15 EXAMPLE 24

3-{1-[4-(Indol-3-yl)butanoyl]-piperidin-4-yl}-benzylamine trifluoroacetate

(A.K.A. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-4-(1H-indol-3-yl)-butan-1-one trifluoroacetate)

By proceeding in a similar manner to the method described in EXAMPLE 20, but using 4-(indol-3-yl)butanoic acid in place of indole-6-carboxylic acid, there was prepared the title compound as a yellow oil. LC-MS: R_T = 3.64 minutes (>90% by ELSD); MS (ES⁺), 376(MH⁺).

EXAMPLE 25

3-{1-[4-(4-Biphenyl)-4-ketobutanoyl]-piperidin-4-yl}-benzylamine trifluoroacetate

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-biphenyl-4-yl-methanone trifluoroacetate)

By proceeding in a similar manner to the method described in EXAMPLE 20, but using 4-(4-biphenyl)-4-ketobutanoic acid in place of indole-6-carboxylic acid, there was prepared the title compound as a yellow oil. LC-MS: R_T = 4.00 minutes (100% by ELSD); MS (ES⁺), 427(MH⁺).

EXAMPLE 26

3-[1-(3-Benzyloxybenzoyl)-piperidin-4-yl]-benzylamine trifluoroacetate
 (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(3-benzyloxy-phenyl)-methanone
 trifluoroacetate)

 By proceeding in a similar manner to the method described in EXAMPLE 23, but using 3-benzyloxybenzoic acid in place of indole-6-carboxylic acid, there was prepared the title compound as a yellow oil. LC-MS: R_T = 3.87 minutes (100% by ELSD); MS (ES⁺), 401 (MH⁺).

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EXAMPLE 27

3-[1-(5-Phenylethynyl-thiophene-2-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(5-phenylethynyl-thiophen-2-yl)-methanone trifluoroacetate)

By proceeding in a similar manner to the method described in EXAMPLE 20, but using 5-phenylethynyl-thiophene-2-carboxylic acid in place of indole-6-carboxylic acid, there was prepared the title compound as a yellow oil. LC-MS: $R_T = 4.09$ minutes (>97% by ELSD); MS(ES⁺), 410(MH⁺).

10 EXAMPLE 28

3-[1-(4-Phenylethynyl-thiophene-2-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(4-phenylethynyl-thiophen-2-yl)-methanone trifluoroacetate)

By proceeding in a similar manner to the method described in EXAMPLE 20, but using 4-phenylethynyl-thiophene-2-carboxylic acid in place of indole-6-carboxylic acid, there was prepared the title compound as a yellow oil. LC-MS: $R_T = 4.08$ minutes (>96% by ELSD); MS(ES⁺), 401(MH⁺).

EXAMPLE 29

3-(1-Benzoyl-piperidin-4-yl)-benzylamine trifluoroacetate

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-phenyl-methanone trifluoroacetate)

By proceeding in a similar manner to the method described in EXAMPLE 20, but using benzoic acid in place of indole-6-carboxylic acid, there was prepared the <u>title compound</u> as a yellow oil. LC-MS:

R_T = 3.39 minutes (>95% by ELSD); MS(ES⁺) 295(MH⁺).

25 EXAMPLE 30

3-[1-(4-N,N-Dimethylaminobenzoyl)-piperidin-4-yl]-benzylamine trifluoroacetate (A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(4-dimethylamino-phenyl)-methanone trifluoroacetate)

By proceeding in a similar manner to the method described in EXAMPLE 20, but using 4-N,N-dimethylaminobenzoic acid in place of indole-6-carboxylic acid, there was prepared the <u>title</u> compound as a yellow oil. LC-MS: $R_T = 3.32$ minutes (100% by ELSD); MS(ES⁺) 338(MH⁺).

EXAMPLE 31

6-Fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride

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(A.K.A. [4-(3-Aminomethyl-4-fluoro-phenyl)-piperidin-1-yl]-(5-phenethyl-pyridin-3-yl)-methanone di-hydrochloride)

By proceeding in a similar manner to the method described in EXAMPLE 17, but using 3-bromo-6-fluoro-benzylamine in place of 3-bromo-4-fluoro-benzylamine, there was prepared the <u>title compound</u> as a pale yellow oil. ¹H NMR [(CD₃)₂SO, 500 MHz]: δ 8.44 (m, 2H), 7.61 (s, 1H), 7.40 (m, 1H), 7.20 (m, 6H), 7.05 (m, 1H), 4.62 (br m, 1H), 3.98 (m, 2H), 3.45 (br m, 1H), 3.20 (br m, 1H), 3.07 (m, 2H), 3.00 (m, 2H), 2.95 (m, 2H) 1.80 (br m, 1H), 1.70 (br m, 3H). MS(EI): 418(M⁺+H).

EXAMPLE 32

10 1-{3-[1-(5-Phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-phenyl)ethylamine di-hydrochloride (A.K.A. {4-[3-(1-Amino-ethyl)-phenyl]-piperidin-1-yl}-(5-phenethyl-pyridin-3-yl)-methanone di-hydrochloride)

By proceeding in a similar manner to the method described in EXAMPLE 17, but using 1-(3-bromophenyl)ethylamine (prepared according to the procedure of C.P.Chen et al., Tetrahedron Letters, 199, 32(49), pages 7175-7178) in place of 3-bromo-4-fluoro-benzylamine, there was prepared the <u>title compound</u> as a white solid. 1 H NMR[(CD₃)₂SO, 500 MHz]: δ 8.62 (m, 2H), 7.95 (s, 1H), 7.50 (s, 1H), 7.20 (m, 8H), 4.62 (br m, 1H), 4.38 (t, J = 6 Hz, 1H), 3.50 (m, 1H), 3.45 (br m, 1H), 3.20 (br m, 1H), 3.07 (m, 2H), 3.00 (m, 2H), 2.95 (m, 2H), 1.87 (br m, 1H), 1.65 (br m, 3H), 1.50 (d, J = 6 Hz, 3H). MS(EI): 414(M⁺+H).

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EXAMPLE 33

3-[1-(4-Hydroxy-quinoline-3-carbonyl)-piperidin-4-yl]-benzylamine

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(4-hydroxy-quinolin-3-yl)-methanone) By proceeding in a similar manner to the method described in EXAMPLE 1, but using 4-hydroxy-quinoline-3-carboxylic acid (prepared according to the procedure of K.J.Shah, and E.A.Coats, J. Med. Chem., 1977, 20(8), pages 1001-1006) in place of 5-phenylethynyl-pyridine-3-carboxylic acid, there was prepared the <u>title compound</u> as a white amorphous solid. ¹H NMR[(CD₃)₂SO, 500 MHz]: δ 8.10 (m, 2H), 7.68 (m, 1H), 7.59 (m, 1H), 7.36 (m, 3H), 7.22 (m, 2H), 4.65 (br m, 1H), 4.00 (m, 2H), 3.80 (br m, 1H), 3.35 (br m, 1H), 3.10 (br m, 1H), 3.00 (br m, 1H), 1.90-1.75 (br m, 4H). MS(EI): 362(M⁺+H).

EXAMPLE 34

3-[1-(6-Phenyl-quinoline-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride

(A.K.A. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(6-phenyl-quinolin-3-yl)-methanone di-hydrochloride)

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By proceeding in a similar manner to the method described in EXAMPLE 1, but using 6-phenyl-quinoline-3-carboxylic acid [prepared according to the procedure of J.Biwersi et al., Am. J. Physiol., 1992, 262(1, Pt. 1), C243-C250] in place of 5-phenylethynyl-pyridine-3-carboxylic acid, there was prepared the <u>title compound</u> as a white amorphous solid. ¹H NMR[(CD₃)₂SO, 500 MHz]: δ 9.00 (s, 1H), 8.59 (s, 1H), 8.41 (s, 1H), 8.10 (m, 2H), 7.85 (m, 2H), 7.58 (m, 2H), 7.45 (m, 2H), 7.34 (m, 3H), 4.75 (br m, 1H), 4.00 (m, 2H), 3.80 (br m, 1H), 3.35 (br m, 1H), 3.00 (br m, 1H), 2.90 (br m, 1H), 1.90-1.75 (br m, 4H). MS(EI): 422(M⁺+H).

EXAMPLE 35

4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-4-carbonitrile

A. 3-Cyanobenzylcyanide

To a solution of 9.8g (200 mmole) of sodium cyanide and 1.61g (5 mmole) of tetrabutylammonium bromide in 50 ml of water was added a solution of 19.61g (100 mmole) of α-bromo-m-tolunitrile in 150 ml of dichloromethane. The mixture was stirred at room temperature for 24 hours. To this mixture was added 6.2 ml (100 mmole) of iodomethane. The mixture was stirred at room temperature for 3 hours. The layers were separated and the organic layer was dried over magnesium sulfate and was filtered. The filtrate was evaporated and the residue was triturated with petroleum ether and the insoluble material was collected to give 14.5g of a white solid, mp-66-9°C; 100% yield: ¹H-NMR (300 MHz, CDCl₃) δ (TMS) 3.80-3.90(s, 2H), 7.49-7.72(m, 4H).

B. N-tert-Butoxycarbonyl-bis(2-chloroethyl)amine

To a mixture of 17.85g (100 mmole) of bis(2-chloroethyl)amine hydrochloride and 24.0g (110 mmole) of di-*tert*-butyl dicarbonate in 100 ml of dichloromethane was added a solution of 15.3 ml (110 mmole) of trietylamine in 50 ml of dichloromethane dropwise over 30 minutes. The mixture was stirred at room temperature for 24 hours and was poured into water. The organic layer was dried over magnesium sulfate and was filtered. The filtrate was evaporated to give 24g of an oil, 100% yield: ¹H-NMR (300 MHz, CDCL₃) δ (TMS) 1.37-1.56 (m, 9H), 3.50-3.62 (m, 8H); MS (ESI) m/e 242 (M+H)⁺.

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C. 4-(3-Cyanophenyl)-1-tert-butoxycarbonyl-piperidine-4-carbonitrile

To a solution of 2.8g (19.7 mmole) of 3-cyanobenzylnitrile and 4.77g (19.7 mmole) of N-tert-butylcarbonyl-bis(2-chloroethyl)amine in 100 ml of anhydrous DMF was added 2.36g (59.1 mmole) of 60% sodium hydride in portions over 10 minutes. The mixture was stirred at room temperature for 3 days and was poured into water and was extracted with ether. The ether layer was dried over magnesium sulfate and was filtered. The filtrate was evaporated and the residue was purified by flash

chromatography using 4:1 hexane:ethyl acetate to give the product as a white solid: 1 H-NMR (300 MHz, CDCl₃) δ (TMS) 1.45(s, 9H), 1.85-2.0(m, 2H), 2.0-2.28(m, 2H), 3.05-3.30(m, 2H), 4.12-4.4(m, 2H), 7.53-7.80(m, 4H).

5 D. 4-(3-Aminomethyl-phenyl)-1-tert-butoxycarbonyl-piperidine-4-carbonitrile

To a mixture of 0.31g (1 mmole) of 4-(3-cyanophenyl)-1-tert-butoxycarbonyl-piperidine-4-carbonitrile in 30 ml of absolute ethanol was added 0.08ml (1 mmole) of conc. hydrochloric acid followed by 30mg of 5% Pd/C. The mixture was agitated in a Parr shaker for 3 hours at 30 lbs. of pressure of hydrogen. The mixture was filtered through celite and the filtrate was evaporated. The residue was treated with ether and was stirred for 30 minutes and was filtered. The filter cake was treated with aqueous sodium carbonate and was extracted with dichloromethane to give 0.2g of product: ¹H-NMR (300 MHz, CDCl₃) δ(TMS) 1.38-1.60(m, 9H), 1.88-2.18(m, 4H), 3.05-3.30(m, 4H), 3.79-4.0(m, 2H), 7.22-7.85(m, 4H); MS (ESI) m/e 316 (M+H)⁺.

E. 4-(3-Benzyloxycarbonylaminomethyl-phenyl)-1-tert-butoxycarbonyl-piperidine-4-carbonitrile
 To a solution of 0.2g of 4-(3-Aminomethyl-phenyl)-1-tert-butoxycarbonyl-piperidine-4-carbonitrile in
 15 ml of dichloromethane was added a few drops of triethylamine followed by a few drops of benzyl
 chloroformate. The mixture was stirred for 1 hour at room temperature and was poured into aqueous
 sodium carbonate and was extracted with dichloromethane. The organic layer was dried over
 magnesium sulfate and was filtered. The filtrate was evaporated and the residue was used directly in
 the next step without further purification: ¹H-NMR (300 MHz, CDCL₃) δ (TMS) 1.39-1.52 (m, 9H),
 1.80-2.16(m, 4H), 3.08-3.42(m, 4H), 4.19-4.50(m, 2H), 5.08-5.13(d, 2H), 7.28-7.79(m, 9H); MS (ESI)
 m/e 450 (M+H)⁺.

25 F. 4-(3-Benzyloxycarbonylaminomethyl-phenyl)-piperidine-4-carbonitrile

The residue from the previous step was dissolved in dichloromethane containing 1 ml of trifluoroacetic acid and the solution was stirred at room temperature for 45 minutes. The solution was poured into aqueous sodium carbonate and was extracted with dichloromethane. The organic layer was dried and evaporated and the residue was purified by flash chromatography using 7:3 hexane:ethyl acetate to give the product: ¹H-NMR (300 MHz, CDCL₃) δ (TMS) 1.80-2.18(m, 4H), 3.07-3.35(m, 4H), 4.28-4.50(m, 2H), 5.09-5.13(d, 2H), 7.10-7.77(m, 9H); MS (ESI) m/e 349 (M+H)⁺.

G. 4-(3-Benzyloxycarbonylaminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-4-carbonitrile

To a solution of 0.15g (0.33 mmole) of 4-(3-benzyloxycarbonylaminomethyl-phenyl)-piperidine-4carbonitrile in 20 ml of acetonitrile was added 0.038g (0.33 mmole) of N-ethylmopholine followed by

0.11g (0.33 mmole) of TBTU. To this solution was added 0.075g (0,33 mmole) of 5-phenethylpyridine-3-carboxylic acid in portions over 10 minutes. The mixture was stirred for 2 hours. The solution was concentrated and the residue was purified by flash chromatography using 95:5 dichloromethane:methanol to provide 0.2g of product: ¹H-NMR (300 MHz, CDCL₃) δ (TMS) 1.79-2.20 (m, 4H), 2.70-2.82 (m, 4H), 2.90-3.07 (m, 2H), 3.15-3.70 (m, 2H), 4.35-4.40 (d, 2H), 5.07-5.25 (d, 2H), 7.10-7.50 (m, 15H), 8.42-8.58 (m, 2H); MS (ESI) m/e 559 (M+H)⁺.

H. 4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-4-carbonitrile
To a solution of 0.15g of 4-(3-benzyloxycarbonylaminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-4-carbonitrile in 5 ml of glacial acetic acid was added 1 ml of 30% HBr in acetic acid. The solution was stirred at room temperature for 2 hours. The solution was poured into a saturated sodium carbonate solution and was extracted with dichloromethane. The organic layer was dried over magnesium sulfate and was filtered and evaporated. The residue was purified by Rainin HPLC using 10-100% (acetonitrile-0.1% aqueous TFA) to yield 16 mg of product isolated as the trifluoroacetic acid salt: H-NMR (300 MHz, DMSO-d⁶) δ (TMS); 1.95-2.30 (m, 4H), 2.45-2.62(m, 2H), 2.88-3.12(m, 4H), 3.70-4.20 (m, 2H), 7.12-7.38(m, 4H), 7.45-7.82(m, 6H), 8.50-8.65(m, 2H); MS (ESI) m/e 425 (M+H)⁺.

EXAMPLE 36

[4-(3-Aminomethylphenyl)piperidin-1-yl]-(3,4-dichlorophenyl)methanone trifluoroacetate TFP resin (125mg of 1.25mmol/g resin, with 100% loading of acid, 156mmol, prepared according to the procedure described by J.M.Salvino et. al. in International Patent Application Publication No. WO 99/67228) was swollen in dichloromethane (2.5mL) for 15 minutes then treated with a solution of 4-(3-aminomethylphenyl)piperidine (40mg, 100mmol) in dichloromethane (2.5mL). The mixture was sealed in the reaction vessel then left shaking for 8 hours. The resin was filtered, then washed with dichloromethane (2mL) [TLC (5% MeOH / EtOAc) showed single product spot (no baseline amine)] and then treated with trifluoroacetic acid (0.5mL). After shaking for 2 hours TLC showed no residual intermediate and the reaction mixture was evaporated. The residue [97% purity by HPLC: $R_T = 7.32$ minutes; 10 micron C_{18} reverse phase column (4.6mm x 10cm) eluting with 10-100% acetonitrile and water containing 0.1%trifluoroacetic acid] was dissolved in water (50mL) and the solution was lyophilized to give the title compound as an amorphous solid. 1 H NMR [(CD₃)₂SO]: δ 8:15 (br s, 3H), 7.72-7.69 (m, 2H), 7.40 (dd, 1H), 7.36-7.25 (m, 4H), 4.66-4.51 (m, 1H), 4.05-3.96 (m, 2H), 3.69-3.48 (m, 1H), 3.30-3.11 (m, 1H), 2.91-2.73 (m, 2H), 1.90-1.54 (m, 4H). MS(Ion spray): 363 and $^{365}(M^{+}+1)$.

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EXAMPLE 37

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1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(2-phenoxy-phenyl)-methanone trifluoroacetate
By proceeding in a similar manner to the method described in EXAMPLE 36, but using the 2phenoxybenzoic acid derived TFP resin in place of the 3,4-dichlorobenzoic acid TFP resin, there was
prepared the <u>title compound</u> as a white amorphous solid. ¹H NMR [(CD₃)₂SO]: δ 8.11 (br s, 3H,
NH₃⁺); 7.43-7.04 (m, 10H); 7.02-6.85 (m, 3H); 4.65-4.52 (m, H); 4.05-3.90 (m, 2H); 3.62-3.49 (m, H);
3.21-3.05 (m, H); 2.86-2.66 (m, 2H); 1.87-1.30 (m, 4H). MS(Ion spray): 587 (M⁺+1).

EXAMPLE 38

1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-methylsulfanyl-6,7-dihydro-5Hbenzo[c]thiophen-4-one trifluoroacetate 2-(1H-Benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU) (120mg, 0.38mmol) was added to a room temperature solution of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydrobenzo[c]thiophene-1-carboxylic acid (88mg, 0.36mmol) and diisopropylethylamine (140mg, 1.08mmol) in dimethylformamide (2mL), under nitrogen. The reaction mixture was stirred for 10 minutes at room temperature before adding a solution of 4-[3-(N,N-di-tertbutoxycarbonylaminomethyl)phenyl]piperidine (140mg, 0.36mmol) and diisopropylethylamine (140mg, 1.08mmol) in dimethylformamide (2mL). The reaction mixture was stirred at room temperature for 16 hours, concentrated to dryness in vacuo, and subjected to dry flash column chromatography on silica with 50:50, dichloromethane:ethyl acetate. 1-{1-[4-(3-(N,N-di-tertbutoxycarbonylaminomethyl)phenyl)-piperidin-1-yl]-methanoyl}-3-methylsulfanyl-6,7-dihydro-5Hbenzo[c]thiophen-4-one was isolated as a colorless oil (177mg). The intermediate was dissolved in dichloromethane (20mL), cooled at 0°C, and treated with trifluoroacetic acid (2mL). The reaction mixture was stirred at room temperature under nitrogen for 2 hours, and concentrated to dryness in vacuo. The residue was dissolved in 20% acetonitrile/water [containing 0.1% trifluoroacetic acid] (9mL) and purified by preparative reverse-phase HPLC (C-18, 10 micron reverse-phase column), eluting with 10% to 100% acetonitrile / water (containing 0.1% trifluoroacetic acid). The product fractions were combined and the acetonitrile removed in vacuo. The aqueous residue was frozen and lyophilized to give the title compound as an amorphous white solid (122mg, 64%). ¹H NMR [(CD₃)₂SO]: δ 8.16 (br s, 3H, NH₃⁺); 7.41-7.24 (m, 4H); 4.21 (br d, 2H); 4.03 (q, 2H); 3.18-3.02 (m, 2H); 2.91-2.72 (m, 3H); 2.59 (s, 3H); 2.53-2.41 (m, 2H); 1.98-1.90 (m, 2H); 1.90-1.79 (m, 2H); 1.68-1.50 (m, 2H). MS(Ion spray): $415 (M^{+}+1)$.

EXAMPLE 39

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(6-chloro-benzo[b]thiophen-2-yl)-methanone trifluoroacetate

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By proceeding in a similar manner to the method described in EXAMPLE 38, but using 6-chlorobenzo[b]thiophene-2-carboxylic acid (prepared according to the procedure described in International Patent Application No. WO 0107436) in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the <u>title compound</u> as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.17 (d, H); 8.14 (br s, 3H, NH₃⁺); 7.91 (d, H); 7.73 (s, H); 7.45 (dd, H); 7.37 (s, H); 7.35-7.24 (m, 3H); 4.42 (br s, 2H); 4.00 (q, 2H); 3.12 (br s, 2H); 2.93-2.79 (m, H); 1.89-1.77 (m, 2H); 1.70-1.55 (m, 2H). MS(Ion spray): 385 and 387 (M⁺+1).

EXAMPLE 40

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-chloro-1H-indol-2-yl)-methanone trifluoroacetate By proceeding in a similar manner to the method described in EXAMPLE 38, but using 5-chloro-1H-indole-2-carboxylic acid in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 11.78 (s, H); 8.14 (br s, 3H, NH₃⁺); 7.63 (s, H); 7.43-7.22 (m, 5H); 7.16 (dd, H); 6.76
(s, H); 4.55 (br d, 2H); 4.00 (q, 2H); 3.14 (br s, 2H); 2.94-2.80 (m, H); 1.90-1.79 (m, 2H); 1.73-1.54 (m, 2H); MS(Ion spray): 368 and 370 (M⁺+1).

EXAMPLE 41

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(8-chloro-4H-1,5-dithia-cyclopenta[a]naphthalen-2-yl)-methanone trifluoroacetate

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 8-chloro-4H-1,5-dithiacyclopenta[a]naphthalene-2-carboxylic acid in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the <u>title compound</u> as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.14 (br s, 3H, NH₃⁺); 7.52 (d, H); 7.44-7.23 (m, 7H); 4.45 (s, 2H); 4.43 (br d, 2H); 4.00 (q, 2H); 3.12 (br s, 2H); 2.95-2.80 (m, H); 1.90-1.78 (m, 2H); 1.72-1.56 (m, 2H). MS(Ion spray): 453 and 455 (M⁺+1).

EXAMPLE 42

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(2',4'-difluoro-4-hydroxy-biphenyl-3-yl)-methanone trifluoroacetate

By proceeding in a similar manner to the method described in EXAMPLE 38, but using diflunisal in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the <u>title compound</u> as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 10.15 (s, H, OH); 8.15 (br s, 3H, NH₃⁺); 7.56-7.46 (m, H); 7.40-7.22 (m, 7H); 7.13 (td, H); 6.97 (d, H); 4.64 (br s, H);

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3.98 (q, 2H); 3.51 (br s, H); 3.10 (br s, H); 2.88-2.71 (m, H); 1.90-1.46 (m, 4H). MS(Ion spray): 423 and 424 (M⁺+1).

EXAMPLE 43

5 <u>l-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-methylsulfanyl-6,7-dihydro-benzo[c]thiophen-1-yl)-methanone trifluoroacetate</u>

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 3-methylsulfanyl-6,7-dihydro-benzo[c]thiophene-1-carboxylic acid in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the <u>title compound</u> as an amorphous white solid. ¹H NMR [CDCl₃]: δ 8.13 (br s, 3H, NH₃⁺); 7.38-7.30 (m, H); 7.27-7.18 (m, 3H); 6.68 (d, H); 6.11-6.04 (m, H); 4.52-4.25 (br m, 2H); 4.01-3.93 (br m, 2H); 3.40-3.38 (m, H); 3.12-2.97 (m, H); 2.90-2.75 (m, H); 2.75 (t, 2H); 2.43 (s, 3H); 2.37-2.28 (m, 2H); 1.97-1.81 (m, 2H); 1.89-1.60 (m, 2H). MS(Ion spray): 400 (M⁺+1).

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EXAMPLE 44

 $\underline{1-\{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl\}-6,6-dimethyl-3-methylsulfanyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate}$

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 6,6-dimethyl-3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.16 (br s, 3H, NH₃⁺); 7.40-7.34 (m, 2H); 7.32-7.26 (m, 2H); 4.20 (br d, 2H); 4.01 (br s, 2H); 3.20-3.06 (m, 2H); 2.93-2.80 (m, H); 2.67 (s, 2H); 2.60 (s, 3H); 2.38 (3, 2H); 1.89-1.78 (m, 2H); 1.67-1.50 (m, 2H); 0.98 (s, 6H). MS(Ion spray): 444 (M⁺+1).

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EXAMPLE 45

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(6-bromo-pyridin-3-yl)-methanone bistrifluoroacetate

A. 6-Bromonicotinic acid hydrochloride

n-Butyllithium (8.0 mL of 2.5M in hexanes, 20 mmol) was added dropwise to a stirring solution of 2,5-dibromopyridine (4.74 g, 20 mmol) in THF (100 mL) at -100 °C, under nitrogen. The reaction mixture was left at this temperature for 30 minutes before bubbling anhydrous carbon dioxide gas through the reaction mixture (for 20 minutes), and leaving to warm to-20 °C. Quenched with 1N HCl (20 mL) and brine (20 mL), and extracted into ethyl acetate, dried over magnesium sulfate, concentrated to dryness. 6-Bromonicotinic acid hydrochloride was isolated as a pale yellow powder

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(3.8 g, 16 mmol). ¹H NMR [CDCl₃+CD₃OD]: δ 8.86 (d, 1H), 8.07 (dd, 1H), 7.52 (d, 1H). MS(Ion spray): 202 and 204 (M⁺+1).

B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(6-bromo-pyridin-3-yl)-methanone bistrifluoroacetate

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 6-bromonicotinic acid hydrochloride in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydrobenzo[c]thiophene-1-carboxylic acid, there was prepared the <u>title compound</u> as an amorphous white solid. ¹H NMR [CD₃OD]: δ 8.48 (d, H); 7.89 (dd, H); 7.82 (d, H); 7.48-7.30 (m, 4H); 4.90-4.81 (m, H); 4.15 (s, 2H); 3.84 (br d, H); 3.46-3.36 (m, H); 3.11-2.91 (m, 2H); 2.13-1.68 (m, 4H). MS(Ion spray): 374 and 376 (M⁺+1).

EXAMPLE 46

6-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-2,3-dihydro-thiazolo[3,2-a]pyrimidin-5-one

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 5-oxo-2,3-dihydro-5H-thiazolo[3,2-a]pyrimidine-6-carboxylic acid in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [CD₃OD]: δ 7.97 (s, H); 7.44-7.29 (m, 4H); 4.76 (br d, H); 4.59-4.51 (m, 2H); 4.07 (s, 2H); 3.83 (br d, H); 3.69-3.57 (m, 2H); 3.41-3.21 (m, H); 3.02-2.85 (m, 2H); 2.05-1.67 (m, 4H). MS(Ion spray): 371 (M⁺+1).

EXAMPLE 47

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-chloro-phenyl)-methanone trifluoroacetate

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 3-chlorobenzoic acid in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.14 (br s, 3H, NH₃⁺); 7.57-7.43 (m, 3H); 7.40-7.22 (m, 5H); 4.70-4.56 (m, H); 4.01 (q, 2H); 3.64-3.56 (m, H); 3.23-3.10 (m, H); 2.91-2.79 (m, 2H); 1.92-1.52 (m, 4H). MS(Ion spray): 329 and 331 (M⁺+1).

EXAMPLE 48

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(4-chloro-phenyl)-methanone trifluoroacetate

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 4chlorobenzoic acid in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-

carboxylic acid, there was prepared the <u>title compound</u> as an amorphous white solid. ^{1}H NMR [(CD₃)₂SO]: δ 8.15 (br s, 3H, NH₃⁺); 7.53 (d, 2H); 7.44 (d, 2H); 7.40-7.23 (m, 4H); 4.64-4.56 (m, H); 4.02 (q, 2H); 3.72-3.58 (m, H); 3.24-3.10 (m, H); 2.95-2.89 (m, 2H); 1.90-1.50 (m, 4H). MS(Ion spray): 329 and 331 (M⁺+1).

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EXAMPLE 49

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[5-(2-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-methanone trifluoroacetate

A. 3-[5-(2-Chlorophenyl)-[1,3,4]oxadiazol-2-yl]-benzoic acid methyl ester
3-(2H-Tetrazol-5-yl)-benzoic acid methyl ester (204mg, 1mmol) (prepared by the method of Tanaka et al, J. Med. Chem., 1998, 41(13), 2406) and 2-chlorobenzoyl chloride (175mg, 1mmol) were combined in anisole (10mL) at room temperature and 2,4,6-collidine (121mg, 1mmol) in anisole (1mL) was added. The reaction mixture was heated at 100°C for 1 hour followed by 120°C for 15 minutes,
monitoring the evolution of gas by balloon [volume of gas evolved was measured by positive displacement of water, total = 22mL]. Cooled reaction mixture to room temperature, and concentrated to dryness in vacuo. The residue was subjected to flash column chromatography on silica with gradient dilution 5% to 40% ethyl acetate / heptane. 3-[5-(2-Chlorophenyl)-[1,3,4]oxadiazol-2-yl]-benzoic acid methyl ester was isolated as a colorless powder (229mg, 73%). ¹H NMR [CDCl3]: δ 8.79 (s, H); 8.36
(d, H); 8.25 (d, H); 8.14 (d, H); 7.72-7.57 (m, 2H); 7.57-7.41 (m, 2H); 4.00 (s, 3H). MS(Ion spray): 315 and 317 (M⁺+1).

B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[5-(2-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-methanone trifluoroacetate

1N Sodium hydroxide (2mL, 2mmol) was added to a solution of 3-[5-(2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-benzoic acid methyl ester (113mg, 0.36mmol) in methanol (5mL) and THF (2mL), and the reaction mixture stirred at room temperature for 2h, before neutralizing to pH 7 with 1N hydrochloric acid. The solution was concentrated to dryness in vacuo and placed under high vacuum overnight. Crude material was used directly without purification [MS(Ion spray): 301 and 303 (M+1); LC/MS purity > 95%, only major impurity is sodium chloride]. 2-(1H-Benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU) (116mg, 0.36mmol) was added to a room temperature solution / suspension of crude 3-[5-(2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-benzoic acid and diisopropylethylamine (150mg, 1.14mmol) in dimethylformamide (2mL), under nitrogen. The reaction mixture was stirred for 10 minutes at room temperature before adding a solution of 4-[3-(N,N-di-tert-butoxycarbonylaminomethyl)phenyl]piperidine (78mg, 0.2mmol) and diisopropylethylamine

(150mg, 1.14mmol) in dimethylformamide (2mL). The reaction mixture was stirred at room temperature for 16 hours, concentrated to dryness in vacuo, and subjected to dry flash column chromatography on silica with 50:50, dichloromethane:ethyl acetate. 1-{4-[3-(N,N-di-tert-butoxycarbonylaminomethyl)phenyl]-piperidin-1-yl}-1-{3-[5-(2-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-methanone was isolated as a colorless oil, which was dissolved in dichloromethane (10mL), cooled at 0°C, and treated with trifluoroacetic acid (1mL). The reaction mixture was stirred at room temperature under nitrogen for 2 hours, and concentrated to dryness in vacuo. The residue was dissolved in 20% acetonitrile/water [containing 0.1% trifluoroacetic acid] (9mL) and purified by preparative reverse-phase HPLC (C-18, 10 micron reverse-phase column), eluting with 20% to 60% acetonitrile / water (containing 0.1% trifluoroacetic acid). The product fractions were combined and concentrated to dryness in vacuo. The title compound was isolated as an amorphous white glass solid (98mg, 83%). H NMR [(CD₃)₂SO]: 8 8.16 (br s, 3H, NH₃⁺) overlapped with 8.22-8.16 (m, 2H) and 8.13 (s, H); 7.79-7.72 (m, 3H); 7.69 (td, H); 7.62 (td, H); 7.41 (s, H); 7.39-7.27 (m, 3H); 4.64 (br d, H); 4.03 (q, 2H); 3.79-3.63 (m, H); 3.28-3.20 (m, H); 3.03-2.80 (m, 2H); 1.96-1.57 (m, 4H). MS(Ion spray): 473 and 475 (M⁺+1).

EXAMPLE 50

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)-phenyl]-methanone bistrifluoroacetate

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A. 3-(5-Pyridin-3-yl-[1,3,4]oxadiazol-2-yl)-benzoic acid methyl ester

Prepared in a similar manner to the method described in EXAMPLE 49A, but using nicotinoyl chloride hydrochloride instead of 2-chlorobenzoyl chloride, 2mmol of 2,4,6-collidine, and heating at 110°C instead of 100°C. The residue was subjected to flash column chromatography on silica with ethyl acetate and 5% methanol / ethyl acetate. 3-(5-Pyridin-3-yl-[1,3,4]oxadiazol-2-yl)-benzoic acid methyl ester was isolated as a colorless powder (84mg, 30%). ¹H NMR [CDCl₃]: δ 9.40 (s, H); 8.84-8.80 (m, H); 8.80-8.78 (m, H); 8.47 (dt, H); 8.38 (dt, H); 8.26 (dt, H); 7.67 (t, H); 7.52 (dd, H); 4.00 (s, 3H). MS(Ion spray): 282 (M⁺+1).

B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)-phenyl]-methanone bistrifluoroacetate

By proceeding in a similar manner to the method described in EXAMPLE 49B, but using 3-(5-pyridin-3-yl-[1,3,4]oxadiazol-2-yl)-benzoic acid methyl ester in place of 3-[5-(2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-benzoic acid methyl ester, there was prepared the <u>title compound</u> as an amorphous white glass solid. ¹H NMR [(CD₃)₂SO]: δ 9.37 (br s, H); 8.86 (br s, H); 8.55 (d, H); 8.28-

8.23 (m, H); 8.20 (s, H); 8.16 (br s, 3H, NH₃⁺); 7.79-7.65 (m, 3H); 7.41 (s, H); 7.39-7.26 (m, 3H); 4.63 (br d, H); 4.09-4.00 (m, 2H); 3.80-3.62 (m, H); 3.37-3.16 (m, H); 3.02-2.80 (m, 2H); 1.98-1.55 (m, 4H). MS(Ion spray): 441 (M⁺+1).

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EXAMPLE 51

1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-ethylsulfanyl-6,6-dimethyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate

By proceeding in a similar manner to the method described in EXAMPLE 49B, but using 3-ethylsulfanyl-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid methyl ester in place of 3-[5-(2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-benzoic acid methyl ester, there was prepared the title compound as an amorphous white glass solid. 1 H NMR [(CD₃)₂SO]: δ 8.16 (br s, 3H, NH₃⁺); 7.40-7.33 (m, 2H); 7.32-7.26 (m, 2H); 4.30-4.00 (m, 4H); 3.21-3.10 (m, 2H); 3.06 (q, 2H); 2.92-2.80 (m, H); 2.66 (s, 2H); 2.38 (s, 2H); 1.90-1.78 (m, 2H); 1.68-1.50 (m, 2H); 0.98 (s, 6H). MS(Ion spray): 458 (M⁺+1).

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EXAMPLE 52

1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-propylsulfanyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate

By proceeding in a similar manner to the method described in EXAMPLE 49B, but using 4-oxo-3-propylsulfanyl-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid ethyl ester in place of 3-[5-(2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-benzoic acid methyl ester, there was prepared the <u>title compound</u> as an amorphous white glass solid. 1 H NMR [(CD₃)₂SO]: δ 8.14 (br s, 3H, NH₃⁺); 7.41-7.23 (m, 4H); 4.21 (br d, 2H); 4.08-3.99 (m, 2H); 3.39-2.99 (m, 4H); 2.94-2.71 (m, 3H); 2.54-2.49 (m, 2H); 2.02-1.90 (m, 2H); 1.90-1.70 (m, 4H); 1.70-1.51 (m, 2H); 1.03 (t, 3H). MS(Ion spray): 443 (M⁺+1).

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EXAMPLE 53

 $\frac{1-\{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl\}-3-isopropylsulfanyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate}$

By proceeding in a similar manner to the method described in EXAMPLE 49B, but using 3-isopropylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid ethyl ester in place of 3-[5-(2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-benzoic acid methyl ester, there was prepared the <u>title compound</u> as an amorphous white glass solid. ¹H NMR [(CD₃)₂SO]: δ 8.14 (br s, 3H, NH₃⁺); 7.43-7.23 (m, 4H); 4.30-4.16 (m, 2H); 4.09-3.98 (m, 2H); 3.53 (septet, H); 3.22-3.03 (m, 2H); 2.93-2.72 (m, 3H); 2.54-2.47 (m, 2H); 2.02-1.86 (m, 4H); 1.70-1.51 (m, 2H); 1.42 (d, 6H). MS(Ion spray): 443 (M⁺+1).

EXAMPLE 54

- 3-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-5,5-dimethyl-7-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carbonitrile trifluoroacetate
- By proceeding in a similar manner to the method described in EXAMPLE 49B, but using 3-cyano-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid ethyl ester in place of 3-[5-(2-chlorophenyl)-[1,3,4]oxadiazol-2-yl]-benzoic acid methyl ester, there was prepared the title compound as an amorphous white glass solid. ¹H NMR [(CD₃)₂SO]: δ 8.14 (br s, 3H, NH₃⁺); 7.41-7.33 (m, 2H); 7.32-7.26 (m, 2H); 4.30-3.90 (br m, 2H); 4.04-3.98 (m, 2H); 3.30-3.01 (m, 2H); 2.93-2.80 (m, H); 2.71
 (s, 2H); 2.54 (s, 2H); 1.89-1.76 (m, 2H); 1.73-1.51 (m, 2H); 1.01 (s, 6H). MS(Ion spray): 423 (M⁺+1).

EXAMPLE 55

- 3-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-5,5-dimethyl-7-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid trifluoroacetate
- The <u>title compound</u> was isolated as a by-product from the reaction carried out to synthesize 3-{1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-5,5-dimethyl-7-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carbonitrile trifluoroacetate, in EXAMPLE 54. ¹H NMR [(CD₃)₂SO]: δ 9.70 (s, H, OH); 8.11 (br s, 3H, NH₃⁺); 7.42-7.26 (m, 4H); 4.28-3.96 (br m, 2H); 4.03-3.99 (m, 2H); 3.27-3.06 (m, 2H); 2.96-2.85 (m, H); 2.70 (s, 2H); 2.63 (s, 2H); 1.93-1.72 (m, 2H); 1.69-1.52 (m, 2H); 1.01 (s, 6H). MS(Ion spray): 442 (M⁺+1).

EXAMPLE 56

- 3-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-5,5-dimethyl-7-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid methyl ester trifluoroacetate
- The <u>title compound</u> was isolated as a by-product from the reaction carried out to synthesize 3-{1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-5,5-dimethyl-7-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carbonitrile trifluoroacetate, in EXAMPLE 54. ¹H NMR [(CD₃)₂SO]: δ 8.16 (br s, 3H, NH₃⁺); 7.41-7.34 (m, 2H); 7.33-7.27 (m, 2H); 4.30-3.95 (br m, 2H); 4.06-4.00 (m, 2H); 3.84 (s, 3H); 3.25-3.04 (m, 2H); 2.94-2.80 (m, H); 2.71 (s, 2H); 2.51 (s, 2H); 1.90-1.78 (m, 2H); 1.71-1.51 (m, 2H); 1.00 (s, 6H). MS(Ion spray): 456 (M⁺+1).

EXAMPLE 57

- $\frac{1-\{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl\}-3-methoxy-6,6-dimethyl-6,7-dihydro-5H-benzo[c]thiophen-4-one.}{5H-benzo[c]thiophen-4-one.}$
- By proceeding in a similar manner to the method described in EXAMPLE 38, but using 3-Methoxy-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the

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title compound as an amorphous white solid. ^{1}H NMR [(CD₃)₂SO]: δ 8.22 (br s, 3H, NH₃⁺), 7.54-7.27 (m, 4H), 4.29-4.22 (m, 2H), 4.14 (s, 3H), 4.13-4.02 (m, 2H), 3.26-3.08 (m, 2H), 3.04-2.86 (m, 1H), 2.71 (s, 2H), 2.37 (s, 2H), 2.02-1.84 (m, 2H), 1.79-1.54 (m, 2H), 1.04 (s, 6H). MS(Ion spray): 427.3 (M⁺+1).

EXAMPLE 58

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(4-pyrrol-1-yl-phenyl)-methanone-trifluoroacetate. By proceeding in a similar manner to the method described in EXAMPLE 38, but using 4-(1H-Pyrrol-1-yl) benzoic acid in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃OD]: δ 7.62-7.51 (m, 4H), 7.41-7.22 (m, 6H), 6.32-6.28 (m, 2H), 4.85-4.66 (m, 2H), 4.08 (s, 2H), 4.03-3.88 (m, 1H), 3.15-2.86 (m, 2H), 2.11-1.62 (m, 4H). MS(Ion spray): 360 (M⁺+1).

EXAMPLE 59

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-benzo[b]thiophen-2-yl-methanone-trifluoroacetate. By proceeding in a similar manner to the method described in EXAMPLE 38, but using benzo(b)-thiophene-2-carboxylic acid in place of 3-methylsulfanyl-4-oxo-4,5,6,7-tetrahydro-benzo[c]thiophene-1-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃OD]: δ 7.98-7.81 (m, 2H), 7.62 (s, 1H), 7.45-7.32 (m, 5H), 7.31-7.22 (m, 1H), 4.80-4.40 (m, 2H), 4.10 (s, 2H), 3.28-3.05 (m, 1H), 3.02-2.90 (m, 2H), 2.02-1.88 (m, 2H), 1.86-1.65 (m, 2H). MS(Ion spray): 351 (M⁺+1).

EXAMPLE 60

(E)-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-(3-methoxy-phenyl)-propenone-trifluoroacetate. By proceeding in a similar manner to the method described in EXAMPLE 38, but using 3-methoxycinnamic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃OD]: δ 7.56 (d, 1H), 7.45-7.25 (m, 5H), 7.23-7.13 (m, 3H), 6.98-6.90 (m, 1H), 4.85-4.70 (m, 1H), 4.50-4.35 (m, 1H), 4.08 (s, 2H), 3.83 (s, 3H), 3.40-3.32 (m, 1H), 3.01-2.75 (m, 2H), 2.08-1.83 (m, 2H), 1.81-1.61 (m, 2H). MS(Ion spray): 351 (M⁺+1).

EXAMPLE 61

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-ethoxy-thiophen-2-yl)-methanone-trifluoroacetate. By proceeding in a similar manner to the method described in EXAMPLE 38, but using 3-ethoxythiophene-2-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃OD]: 8 7.53 (d, 1H), 7.46-7.22 (m, 4H), 6.94 (d, 1H), 4.60-4.21 (br.m., 2H),

4.19 (q, 2H), 4.08 (s, 2H), 3.18-2.98 (m, 1H), 2.96-2.85 (m, 2H), 2.0-1.86 (m, 2H), 1.84-1.65 (m, 2H), 1.37 (t, 3H). MS(Ion spray): 345 (M⁺+1).

EXAMPLE 62

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-2-indan-2-yl-ethanone-trifluoroacetate.

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 2-indanylacetic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃OD]: δ 7.45-7.25 (m, 4H), 7.18-7.15 (m, 2H), 7.14-7.04 (m, 2H), 4.78-4.65 (m, 1H), 4.18-4.11 (m, 1H), 4.08 (s, 2H), 3.28-3.08 (m, 2H), 2.95-2.76 (m, 2H), 2.74-2.58 (m, 6H), 2.01-1.85 (m, 2H), 1.75-1.51 (m, 2H). MS(Ion spray): 349 (M⁺+1).

EXAMPLE 63

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(3-chloro-phenyl)-pyridin-3-yl]-methanone-ditrifluoroacetate.

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A. 5-(3-chlorophenyl)-nicotinic acid

A three neck flask was charged with 5-bromonicotinic acid (2 g, 9.90 mmol), 3-chlorophenylboronic acid (1.55 g, 9.90 mmol), a 0.4 M solution of sodiumcarbonate in water (37 mL, 14.8 mmol) and Acetonitrile (37 mL). The solution was degassed under vacuum and tetrakistriphenylphoshine Pd(0) (0.57 g, 0.495 mmol) was added and the reaction refluxed overnight under nitrogen. The reaction was cooled to room temperature and filtered through a celite pad. The filtrate was partially evaporated under reduced pressure and the remaining solution acidified to pH=2 with 1N HCl. The resulting solid was collected by filtration and dried under vacuum. ¹H NMR [(CD₃)₂SO]: δ 9.15-9.05 (m, 2H), 8.45 (s, 1H), 7.85 (s, 1H), 7.80-7.65 (m, 1H), 7.60-7.42 (m, 2H).

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B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(3-chloro-phenyl)-pyridin-3-yl]-methanone-ditrifluoroacetate.

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 5-(3-chlorophenyl)-nicotinic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.99 (s, 1H), 8.65 (s, 1H), 8.18 (s, 1H), 8.13 (br.s., 3H, NH₃⁺), 7.88 (s, 1H), 7.76 (d, 1H), 7.58-7.45 (m, 2H), 7.40-7.20 (m, 4H), 4.80-4.58 (m, 1H), 3.98 (q, 2H), 3.78-3.55 (m, 1H), 3.33-3.18 (m, 1H), 2.98-2.71 (m, 2H), 1.95-1.52 (m, 4H). MS(Ion spray): 406 (M⁺+1).

EXAMPLE 64

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-chloro-benzo[b]thiophen-2-yl)-methanonetrifluoroacetate.

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By proceeding in a similar manner to the method described in EXAMPLE 38, but using 5-chlorobenzo(b)thiophene-2-carboxylic acid, prepared as in WO 0107436, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.08 (br.s., 3H, NH₃⁺), 8.05 (d, 1H), 8.01 (s, 1H), 7.68 (s, 1H), 7.47 (d, 1H), 7.40-7.21 (m, 4H), 4.41 (br.s., 2H), 3.99, (q, 2H), 3.30-3.15 (m, 2H), 2.95-2.78 (m, 1H), 1.90-1.75 (m, 2H), 1.73-1.52 (m, 2H). MS(Ion spray): 385 (M⁺+1).

EXAMPLE 65

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-2-(3,4-dichloro-phenyl)-ethanone-trifluoroacetate. By proceeding in a similar manner to the method described in EXAMPLE 38, but using 3,4-dichlorophenyl acetic acid, there was prepared the title compound as an amorphous white solid. 1 H NMR [(CD₃)₂SO]: $_{\delta}$ 8.08 (br.s., 3H, NH₃⁺), 7.56 (d, 1H), 7.48 (s, 1H), 7.38-7.15 (m, 5H), 4.58-4.45 (m, 1H), 4.15-3.92 (m, 3H), 3.85-3.65 (m, 2H), 3.18-3.03 (m, 1H), 2.85-2.55 (m, 2H), 1.80-1.65 (m, 2H), 1.55-1.32 (m, 2H). MS(Ion spray): 376 (M⁺+1).

EXAMPLE 66

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-2-(5-chloro-pyridin-3-yloxy)-ethanone-ditrifluoroacetate.

By proceeding in a similar manner to the method described in EXAMPLE 38, but using (5-chloropyridin-3-yloxy)-acetic acid, prepared as in WO 0107436, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.28-8.21 (m, 2H), 8.15 (br.s., 3H, NH₃⁺), 7.58 (s, 1H), 7.40-7.20 (M, 4H), 5.01 (s, 2H), 4.52-4.38 (m, 1H), 3.98 (q, 2H), 3.93-3.80 (m, 1H), 3.22-3.05 (m, 1H), 2.88-2.58 (m, 2H), 1.88-1.35 (m, 4H). MS(Ion spray): 360 (M⁺+1).

EXAMPLE 67

25 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-2-(6-chloro-pyridin-2-yloxy)-ethanone-ditrifluoroacetate.</u>

By proceeding in a similar manner to the method described in EXAMPLE 38, but using (6-chloropyridin-2-yloxy)-acetic acid, prepared as in WO 0107436, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.10 (br.s., 3H, NH₃⁺), 7.81-7.71 (m, 1H), 7.41-7.18 (m, 4H), 7.08 (d, 1H), 6.88 (d, 1H), 5.15-4.92 (m, 2H), 4.50-4.31 (m, 1H), 4.08-3.81 (m, 3H), 3.27-3.08 (m, 1H), 2.92-2.76 (m, 1H), 2.75-2.60 (m, 1H), 1.90-1.58 (m, 2H), 1.57-1.35 (m, 2H). MS(Ion spray): 360 (M⁺+1).

EXAMPLE 68

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(E)-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-(5-chloro-thiophen-2-yl)-propenone-trifluoroacetate.

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 3-(5-chlorothiophen-2-yl)-acrylic acid, prepared as in WO 0107436, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.08 (br.s., 3H, NH₃⁺), 7.56 (d, 1H), 7.40-7.28 (m, 3H), 7.26-7.18 (m, 2H), 7.12 (d, 1H), 6.92 (d, 1H), 4.70-4.50 (m, 1H), 4.41-4.21 (m, 1H), 3.98 (q, 2H), 3.28-3.05 (m, 1H), 2.90-2.63 (m, 2H), 1.91-1.72 (m, 2H), 1.65-1.35 (m, 2H).). MS(Ion spray): 361 (M⁺+1).

10 EXAMPLE 69

(E)-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-(4-chloro-thiophen-2-yl)-propenone-trifluoroacetate.

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 3-(4-chlorothiophen-2-yl)-acrylic acid, prepared as in WO 0107436, there was prepared the title compound as an amorphous white solid. 1 H NMR [(CD₃)₂SO]: $_{2}$ 8 8.06 (br.s., 3H, NH₃⁺), 7.65 (s, 1H), 7.60-7.48 (m, 2H), 7.40-7.20 (m, 4H), 7.08 (d, 1H), 4.70-4.51 (m, 1H), 4.42-4.25 (m, 1H), 4.05-3.93 (m, 2H), 3.28-3.08 (m, 1H), 2.90-2.63 (m, 2H), 1.90-1.65 (m, 2H), 1.63-1.40 (m, 2H). MS(Ion spray): 361 (M⁺+1).

EXAMPLE 70

20 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(4,5,6,7-tetrahydro-benzo[c]thiophen-1-yl)-methanone-trifluoroacetate.</u>

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 4,5,6,7-tetrahydro-benzo(c)thiophene-1-carboxylic acid, prepared as in JOC V62#6 1997 p. 1599, there was prepared the title compound as an amorphous white solid.

¹H NMR [(CD₃)₂SO]: δ 8.13 (br.s., 3H, NH₃⁺), 7.40-7.33 (m, 2H), 7.31-7.25 (m, 2H), 7.20 (s, 1H), 4.35-4.15 (m, 2H), 4.03 (q, 2H), 3.17-2.98 (m, 2H), 2.95-2.78 (m, 1H), 2.73-2.58 (m, 4H), 1.90-1.78 (m, 2H), 1.75-1.63 (m, 4H), 1.61-1.42 (m, 2H). MS(Ion spray): 355 (M⁺+1).

EXAMPLE 71

30 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-chloro-4-methoxy-thiophen-3-yl)-methanone-trifluoroacetate.</u>

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 2-chloro-3-methoxy-thiophene-4-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.13 (br.s., 3H, NH₃⁺), 7.57 (s, 1H), 7.40-7.22 (m, 4H), 4.70-4.58 (m,

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1H), 4.05 (q, 2H), 3.85 (s, 3H), 3.75-3.60 (m, 1H), 3.25 (m, 1H), 2.95-2.78 (m, 2H), 1.93-1.70 (m, 2H), 1.68-1.45 (m, 2H). MS(Ion spray): 365 (M⁺+1).

EXAMPLE 72

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(1H-indol-3-yl)-methanone-trifluoroacetate.
 By proceeding in a similar manner to the method described in EXAMPLE 38, but using Indole-3-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: δ 8.13 (br.s., 3H, NH₃⁺), 7.78-7.63 (m, 2H), 7.52-7.20 (m, 6H), 7.20-7.03 (m, 2H), 4.57-4.38 (m, 2H), 4.03 (q, 2H), 3.17-3.02 (m, 2H), 2.95-2.75 (m, 1H), 1.90-1.78 (m, 2H), 1.75-1.57 (m, 2H). MS(Ion spray): 334 (M⁺+1).

EXAMPLE 73

1-[4-(3-Aminomethyl-phenyl)-4-hydroxy-piperidin-1-yl]-1-(5-phenethyl-pyridin-3-yl)-methanone-ditrifluoroacetate.

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A. 4-(3-Cyano-phenyl)-4-hydroxy-piperidine-1-carboxylic acid-tert-butyl ester.

A solution of 3-Bromobenzonitrile (0.48 g, 2.64 mmol) in THF (20 mL) was stirred under nitrogen at – 78°C. To this was added dropwise a solution of 2.0M nBuLi in hexanes (1.38 mL, 2.72 mmol). The solution was allowed to warm to –15°C over 1.5 hours. The solution was recooled to –78°C and a solution of N-Boc-4-piperidone (0.53 g, 2.64 mmol) in THF (5 mL) was added dropwise. The reaction mixture was allowed to warm to –10°C and stirred at this temperature for three hours. The reaction was quenched with ½ saturated ammonium chloride solution (30 mL) and stirred 15 minutes. The THF was removed by evaporation and the residue extracted with methylene chloride (3 X 50 mL). The organic extracts were combined, dried over sodium sulfate, evaporated to give an orange oil which was purified by flash chromatography 3:5:2 methylene chloride: heptane: ethyl acetate to give the title compound (0.30 g) as a clear oil. ¹H NMR [(CDCl₃]: 8 7.82 (s, 1H), 7.72 (d, 1H), 7.58 (d, 1H), 7.55-7.42 (m, 1H), 4.20-3.95 (m, 2H), 3.35-3.10 (m, 2H), 2.08-1.83 (m, 2H), 1.80-1.66 (m, 2H), 1.51 (s, 9H).

30 B. 4-[3-(Benzyloxycarbonylamino-methyl)-phenyl]-4-hydroxy-piperidine-1-carboxylic acid-*tert*-butyl ester.

A solution of 4-(3-Cyano-phenyl)-4-hydroxy-piperidine-1-carboxylic acid-tert-butyl ester (0.30 g, 0.99 mmol) in 7N ammonia/methanol (25 mL) and 5%Rhodium on alumina (0.15 g) was hydrogenated overnight on a Parr apparatus (45 psi). The reaction was filtered through celite, evaporated, and azeotroped with MeOH:toluene 1:1 (2 X 30 mL) to give 4-(3-Aminomethyl-phenyl)-4-hydroxy-

piperidine-1-carboxylic acid-tert-butyl ester as a foam. This compound was used directly in the next step.

To a stirred mixture of 4-(3-Aminomethyl-phenyl)-4-hydroxy-piperidine-1-carboxylic acid-*tert*-butyl ester (0.30 g, 0.99 mmol), methylene chloride (10 mL) and water (10 mL) was added potassium carbonate (0.28 g, 2.02 mmol) followed by benzylchloroformate (0.34 g, 2.02 mmol). The reaction stirred overnight at room temperature. The reaction was extracted with methylene chloride (3 X 30 mL). The organic extracts were combined, dried over sodium sulfate and evaporated to give a tan oil. Purification by flash chromatography 40% Ethyl acetate: Heptane yielded 4-[3-(Benzyloxycarbonylamino-methyl)-phenyl]-4-hydroxy-piperidine-1-carboxylic acid-*tert*-butyl ester (0.40 g). ¹H NMR [(CDCl₃]: δ 7.45-7.18 (m, 9H), 5.15 (s, 2H), 5.08 (br.s., 1H, NH), 4.40 (d, 2H), 4.15-3.93 (m, 2H), 3.35-3.15 (m, 2H), 2.08-1.90 (m, 2H), 1.75-1.62 (m, 2H), 1.50 (s, 9H).

C.1-[4-(3-Aminomethyl-phenyl)-4-hydroxy-piperidin-1-yl]-1-(5-phenethyl-pyridin-3-yl)-methanone-ditrifluoroacetate.

To a stirred solution of 4-[3-(Benzyloxycarbonylamino-methyl)-phenyl]-4-hydroxy-piperidine-1-carboxylic acid-tert-butyl ester (0.38 g, 0.86 mmol) and methylene chloride (15 mL) at 0°C was added trifluoroacetic acid (5 mL). The reaction was allowed to warm to room temperature, stirred one hour and was evaporated to dryness to give [3-(4-(Hydroxy-piperidin-4-yl)-benzyl]-carbamic acid benzyl ester which was used directly in the next step.

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To a stirred solution of 5-phenethyl-pyridin-3-carboxylic acid (0.027 g, 0.1 mmol) and DMF (10 mL) was added diisopropylethyl amine (0.014 g, 0.11 mmol) followed by TBTU (0.0353 g, 0.11 mmol). This stirred for five minutes before adding a solution of [3-(4-(Hydroxy-piperidin-4-yl)-benzyl]carbamic acid benzyl ester (0.045 g, 0.1 mmol), DMF (2 mL) and Diisopropylethylamine (0.039 g, 0.3 mmol). The reaction stirred overnight at room temperature. The solvent was removed by evaporation and the remaining residue partitioned between ethylacetate (50 mL) and saturated sodium bicarbonate (10 mL). The organic phase was separated, washed again with saturated sodium bicarbonate (10 mL) and dried over magnesium sulfate. Evaporation followed by purification by flash chromatography (100% ethylacetate) gave (3-{4-Hydroxy-1-[-1-(5-phenethyl-pyridin-3-yl)-methanoyl}-piperidin-4-yl}benzyl)-carbamic acid benzyl ester (0.030 g) as a clear oil. Hydrogenation with Methanol (10 mL), Acetic acid (1 mL) and a catalytic amount of 10% Palladium on Carbon overnight followed by filtration through celite gave the crude product which was purified by HPLC as in Example 38 to give the title compound as an amorphous solid (9.1 mg). ¹H NMR [(CD₃)₂SO]: δ 8.58-8.42 (m, 2H), 8.15 (br.s., 3H, NH₃⁺), 7.73 (s, 1H), 7.63-7.51 (m, 2H), 7.40 (t, 1H), 7.38-7.25 (m, 1H), 7.23-7.10 (m, 5H), 4.58-4.38 (m, 1H), 4.03 (q, 2H), 3.60-3.10 (m, 3H), 3.05-2.86 (m, 4H), 2.06-1.80 (m, 2H), 1.78-1.63 (m, 1H), 1.62-1.42 (m, 1H). MS(Ion spray): 416 (M⁺+1).

EXAMPLE 74

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(1-methyl-1H-indol-3-yl)-methanone-trifluoroacetate. By proceeding in a similar manner to the method described in EXAMPLE 38, but using 1-Methyl-1H-indole-3-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [CDCl₃]: δ 8.63 (br.s., 3H, NH₃⁺), 7.60 (d, 1H), 7.51 (s, 1H), 7.41-7.18 (m, 5H), 7.15-7.05 (m, 2H), 4.55-4.35 (m, 2H), 4.01 (br.s., 2H), 3.78 (s, 3H), 3.18-2.95 (m, 2H), 2.80-2.61 (m, 1H), 1.85-1.45 (m, 4H). MS(Ion spray): 348 (M⁺+1).

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EXAMPLE 75

1-(3-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-indol-1-yl)-ethanone-trifluoroacetate. By proceeding in a similar manner to the method described in EXAMPLE 38, but using 1-Acetyl-1H-indole-3-carboxylic acid, there was prepared the title compound as an amorphous white solid. ¹H NMR [(CD₃)₂SO]: 8 8.39 (d, 1H), 8.21 (br.s., 3H, NH₃⁺), 8.13 (s, 1H), 7.70 (d, 1H), 7.68-7.25 (m, 6H), 4.40 (br.s., 2H), 4.15-4.02 (m, 2H), 3.15-3.03 (m, 2H), 2.99-2.80 (m, 1H), 2.71 (s, 3H), 1.95-1.76 (m, 2H), 1.74-1.55 (m, 2H). MS(Ion spray): 376 (M⁺+1).

EXAMPLE 76

20 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-methoxy-1-methyl-1H-indol-3-yl)-methanone-trifluoroacetate.</u>

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 5-Methoxy-1-methyl-1H-indole-3-carboxylic acid, prepared as in WO 9522524, there was prepared the title compound as an amorphous white solid.

¹H NMR [(CD₃)₂SO]: δ 8.13 (br.s., 3H, NH₃⁺), 7.71 (s, 1H), 7.51-7.23 (m, 5H), 7.20 (s, 1H), 6.83 (dd, 1H), 4.53-4.40 (m, 2H), 4.13-3.95 (m, 2H), 3.80 (s, 3H), 3.76 (s, 3H), 3.18-3.01 (m, 2H), 2.95-2.75 (m, 1H), 1.95-1.76 (m, 2H), 1.75-1.52 (m, 2H). MS(Ion spray): 378 (M⁺+1).

EXAMPLE 77

30 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(2-trifluoromethyl-phenyl)-phenyl]-methanone trifluoroacetate</u>

A. 4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidine

As an alternative route, a one-pot cross coupling process was applied to the preparation of the title compound. A solution of 3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-bromobenzene (EXAMPLE

- 1A) (7.7 g, 20 mmol) in anhydrous DMF (60 ml) was treated with potassium acetate (5.9 g, 60 mmol), bis(pinacolato)diboron (5 g, 20 mmol), and [1,1'-bis-(diphenylphosphino) ferroceno]-dichloropalladium (II)-dichloromethane complex (0.49 g, 0.60 mmol). This mixture was stirred at 80°C under an atmosphere of nitrogen for 4 hours, then benzyl 1,2,3,6-tetrahydro-4-
- (trifluoromethylsulphonyloxy)-pyridine-1-carboxylate (EXAMPLE 1B) (9.2 g, crude, < 25 mmol) was added, followed by aq Na₂CO₃ (2M, 60 mL). The mixture was heated at 80°C under an nitrogen for another 2 hours and then concentrated. The cross coupling product (2.2 g) was obtained after purification (as described in EXAMPLE 1B). Further reduction (as described in EXAMPLE 1B) yielded title compound.
- B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(2-trifluoromethyl-phenyl)-phenyl]-methanone trifluoroacetate

By proceeding in a similar manner to the coupling method described in EXAMPLE 5B, but using 2-iodobenzotrifluoride, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. H NMR [CD₃OD]: δ 7.80-7.30 (m, 12H), 4.81 (br, 1H), 4.10 (s, 2H), 3.87 (br 1H), 3.30 (br, 1H), 2.97 (m, 2H), 2.05-1.60 (br, 4H). MS (Ion spray): 463 (M+1).

EXAMPLE 78

 $\frac{1-[4-(3-\mathbf{A}minomethyl-phenyl)-piperidin-1-yl]-1-[3-(2-methyl-phenylethynyl)-phenyl]-methanone}{trifluoroacetate}$

By proceeding in a similar manner to the coupling method described in EXAMPLE 5b, but using 2-iodotoluene, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.66-7.16 (m, 12H), 4.81 (br, 1H), 4.11 (s, 2H), 3.87 (br 1H), 3.30 (br, 1H), 2.97 (m, 2H), 2.51 (s, 3H), 2.05-1.60 (br, 4H). MS (Ion spray): 409 (M+1).

EXAMPLE 79

 $\frac{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(4-chloro-phenylethynyl)-phenyl]-methanone}{trifluoroacetate}$

By proceeding in a similar manner to the coupling method described in EXAMPLE 5b, but using 1-chloro-4-iodobenzene, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.68-7.28 (m, 12H), 4.82 (br, 1H), 4.11 (s, 2H), 3.87 (br 1H), 3.30 (br, 1H), 2.97 (m, 2H), 2.05-1.60 (br, 4H). MS (Ion spray): 429 and 431 (M+1).

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EXAMPLE 80

 $\frac{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(2-chloro-phenylethynyl)-phenyl]-methanone}{trifluoroacetate}$

By proceeding in a similar manner to the coupling method described in EXAMPLE 5b, but using 1-chloro-2-iodobenzene, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.69-7.28 (m, 12H), 4.82 (br, 1H), 4.11 (s, 2H), 3.87 (br 1H), 3.30 (br, 1H), 2.97 (m, 2H), 2.05-1.60 (br, 4H). MS (Ion spray): 429 and 431 (M+1).

10 EXAMPLE 81

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(2-fluoro-phenylethynyl)-phenyl]-methanone trifluoroacetate

By proceeding in a similar manner to the coupling method described in EXAMPLE 5b, but using 1-fluoro-2-iodobenzene, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.69-7.16 (m, 12H), 4.80 (br, 1H), 4.10 (s, 2H), 3.84 (br 1H), 3.30 (br, 1H), 2.96 (m, 2H), 2.05-1.60 (br, 4H). MS (Ion spray): 413 (M+1).

EXAMPLE 82

20 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(3-fluoro-phenylethynyl)-phenyl]-methanone</u> trifluoroacetate

By proceeding in a similar manner to the coupling method described in EXAMPLE 5b, but using 1-fluoro-3-iodobenzene, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.67-7.10 (m, 12H), 4.80 (br, 1H), 4.10 (s, 2H), 3.85 (br 1H), 3.30 (br, 1H), 2.95 (m, 2H), 2.05-1.60 (br, 4H). MS (Ion spray): 413 (M+1).

EXAMPLE 83

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(4-fluoro-phenylethynyl)-phenyl]-methanone trifluoroacetate

By proceeding in a similar manner to the coupling method described in EXAMPLE 5b, but using 1-fluoro-4-iodobenzene, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.64-7.10 (m, 12H), 4.80 (br, 1H), 4.10 (s, 2H), 3.85 (br 1H), 3.30 (br, 1H), 2.97 (m, 2H), 2.05-1.60 (br, 4H). MS (Ion spray): 413 (M+1).

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EXAMPLE 84

 $\frac{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-\{3-[2-(2-fluoro-phenyl)-ethyl]-phenyl\}-methanone}{trifluoroacetate}$

By proceeding in a similar manner to the reduction method described in EXAMPLE 9, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.43-6.96 (m, 12H), 4.78 (br, 1H), 4.11 (s, 2H), 3.72 (br 1H), 3.18 (br, 1H), 3.02-2.86 (m, 6H), 2.05-1.50 (br, 4H). MS (Ion spray): 417 (M+1).

EXAMPLE 85

10 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[2-(3-fluoro-phenyl)-ethyl]-phenyl}-methanone</u> trifluoroacetate

By proceeding in a similar manner to the reduction method described in EXAMPLE 9, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.43-6.80 (m, 12H), 4.78 (br, 1H), 4.11 (s, 2H), 3.70 (br 1H), 3.18 (br, 1H), 3.02-2.85 (m, 6H), 2.05-1.50 (br, 4H). MS (Ion spray): 417 (M+1).

EXAMPLE 86

 $\frac{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-\{3-[2-(4-fluoro-phenyl)-ethyl]-phenyl\}-methanone}{trifluoroacetate}$

By proceeding in a similar manner to the reduction method described in EXAMPLE 9, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.43-6.88 (m, 12H), 4.78 (br, 1H), 4.10 (s, 2H), 3.69 (br 1H), 3.18 (br, 1H), 3.00-2.85 (m, 6H), 2.05-1.50 (br, 4H). MS (Ion spray): 417 (M+1).

25 EXAMPLE 87

 $\frac{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-\{3-[2-(6-amino-pyridin-3-yl)ethynyl]-phenyl\}-1-\{3-[2-(6-amino-pyridin-3-yl)ethynyl]-phenyl$ -1-(3-amino-pyridin-3-yl)ethynyl]-1-\{3-[2-(6-amino-pyridin-3-yl)ethynyl]-1-\{3-[2-(6-amino-pyridin-3-yl)ethynyl]-1-\{3-[2-(6-amino-pyridin-3-yl)ethynyl]-phenyl-1-(3-amino-pyridin-3-yl)ethynyl]-phenyl-1-(3-amino-pyridin-3-yl)ethynyl-1-(3-amino-pyridin-3-yl)ethynyl-1-(3-amino-pyridin-3-yl)ethynyl-1-(3-amino-pyridin-3-yl)ethynyl-1-(3-amino-pyridin-3-yl)ethynyl-1-(3-amino-pyridin-3-yl)ethynyl-1-(3-amino-pyridin-3-yl)ethynyl-1-(3-amino-pyridi

By proceeding in a similar manner to the method described in EXAMPLE 38, but using (6-tert-butoxycarbonylamino-pyridin-3-yl)ethynyl-pyridine-3-carboxylic acid (prepared according to the method described in EXAMPLE 7), the title compound was prepared as an amorphous off-white solid.

¹H NMR [CD₃OD]: δ 8.82 (s, 1H), 8,66 (s, 1H), 8.17 (s, 1H), 8.07 (s, 1H), 8.02 (d, 1H), 7.43-7.27 (m, 4H), 7.05 (d, 1H), 4.81 (br, 1H), 4.10 (s, 2H), 3.79 (br 1H), 3.37 (br, 1H), 2.97 (m, 2H), 2.05-1.70 (br, 4H). MS (Ion spray): 412 (M+1).

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EXAMPLE 88

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[2-(6-amino-pyridin-3-yl)-ethyl]-phenyl}-methanone

tri-trifluoroacetate

By proceeding in a similar manner to the reduction method described in EXAMPLE 9, and the deprotection method described in EXAMPLE 38, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 8.60 (m, 2H), 7.94 (s, 1H), 7.89 (d, 1H), 7.61 (s, 1H), 7.45-7.28 (m, 4H), 6.97 (d, 1H), 4.80 (br, 1H), 4.11 (s, 2H), 3.76 (br 1H), 3.10-2.90 (m, 7H), 2.05-1.60 (br, 4H). MS (Ion spray): 416 (M+1).

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EXAMPLE 89

 $\frac{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(6-chloro-thieno[3,2-b]thiophen-2-yl)-methanone}{trifluoroacetate}$

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 6-chlorothieno[3,2-b]thiophene-2-carboxylic acid, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.60 (s, 1H), 7.47 (s, 1H), 7.33-7.18 (m, 4H), 4.50 (br, 2H), 3.98 (s, 2H), 3.12 (br, 2H), 2.86 (m, 1H), 1.85 (b, 2H), 1.67 (m, 2H). MS (Ion spray): 391 and 393 (M+1).

EXAMPLE 90

20 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-fluoro-thieno[3,2-b]thiophen-2-yl)-methanone</u> trifluoroacetate

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 5-fluoro-thieno[3,2-b]thiophene-2-carboxylic acid, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.65 (s, 1H), 7.44-7.17 (m, 4H), 7.03 (s, 1H), 4.60 (br, 2H), 4.12 (s, 2H), 3.22 (br, 2H), 2.97 (m, 1H), 1.97 (b, 2H), 1.78 (m, 2H). MS (Ion spray): 375 (M+1).

EXAMPLE 91

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-methyl-thieno[3,2-b]thiophen-2-yl)-methanone trifluoroacetate

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 5-methyl-thieno[3,2-b]thiophene-2-carboxylic acid, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.60 (s, 1H), 7.42-7.30 (m, 4H), 7.07 (s, 1H), 4.63 (br, 2H), 4.11 (s, 2H), 3.21 (br, 2H), 2.97 (m, 1H), 2.60 (s, 3H), 1.96 (b, 2H), 1.78 (m, 2H). MS (Ion spray): 371 (M+1).

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EXAMPLE 92

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1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-chloro-thieno[3,2-b]thiophen-2-yl)-methanone trifluoroncetate

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 5-chloro-thieno[3,2-b]thiophene-2-carboxylic acid, the title compound was prepared as an amorphous off-white solid. ¹H NMR [CD₃OD]: δ 7.63 (s, 1H), 7.42-7.29 (m, 5H), 4.60 (br, 2H), 4.11 (s, 2H), 3.12 (br, 2H), 2.97 (m, 1H), 1.97 (b, 2H), 1.78 (m, 2H). MS (Ion spray): 391

In a similar manner to the methods described above, the following compounds are prepared: EXAMPLE 93

10 <u>1-{4-[3-(1-Aminoethyl)phenyl]-piperidin-1-yl}-1-(5-phenylethyl-pyridin-3-yl)-methanone di-</u> hydrochloride

A. [1-(3-Bromophenyl)ethyl]-carbamic acid tert-butyl ester

3-Bromoacetophenone oxime (23.4 mmol) was stirred in glacial acetic acid (150mL) at room temperature under nitrogen, and zinc dust (94mmol) added portionwise. The reaction mixture was stirred at room temperature for 24 hours, filtered off the solids and concentrated the filtrate to dryness. The residue was diluted with water, acidified to pH 5 with 1N HCl, and washed with ethyl acetate. The aqueous was basified with sodium hydrogen carbonate, extracted into ethyl acetate, dried over magnesium sulfate, and concentrated to dryness. The residue was dissolved in dimethylformamide (30mL) and triethylamine (36.9mmol) added. To this solution was added, dropwise, a solution of ditert-butyldicarbonate (32.4mmol) in DMF (10mL). The reaction mixture was stirred at room temperature for 6 hours, and left standing for 24 hours before concentrating to dryness. The residue was partitioned between water and ethyl acetate, and the aqueous phase extracted with ethyl acetate. The combined organic phase was washed with brine, dried over magnesium sulfate, and concentrated to dryness. The residue was purified by column chromatography on silica gel with dichloromethane as eluent, to give [1-(3-bromophenyl)ethyl]-carbamic acid tert-butyl ester as a pale yellow oil which crystallized upon standing, MS(El): 300 and 302 (M⁺+H).

B. 1-{4-[3-(1-Aminoethyl)phenyl]-piperidin-1-yl}-1-(5-phenylethyl-pyridin-3-yl)-methanone dihydrochloride

By proceeding in a manner similar to the method described in EXAMPLE 17D, but using [1-(3-bromophenyl)ethyl]-carbamic acid tert-butyl ester in place of N-(tert-butoxycarbonyl)-3-bromo-4-fluorobenzylamine, there was prepared [1-(3-{1-[1-(3-phenethyl-phenyl)-methanoyl]-1,2,3,6-tetrahydro-pyridin-4-yl}-phenyl)-ethyl]-carbamic acid tert-butyl ester. This material was subjected to the same conditions as described in EXAMPLE 2A, but using [1-(3-{1-[1-(3-phenethyl-phenyl)-methanoyl]-1,2,3,6-tetrahydro-pyridin-4-yl}-phenyl)-ethyl]-carbamic acid tert-butyl ester in place of 5-

phenylethynylpyridine-3-carboxylic acid. The crude product from this reaction was purified by column chromatography on silica gel, before being subjected to the same conditions as described in EXAMPLE 1D, but using [1-(3-{1-[1-(3-phenethylphenyl)-methanoyl]-piperidin-4-yl}phenyl)ethyl]carbamic acid tert-butyl ester in place of 3-[1-(5-phenylethynylpyridine-3-carbonyl)piperidin-4-yl]benzonitrile. 1-{4-[3-(1-Aminoethyl)phenyl]-piperidin-1-yl}-1-(5-phenylethyl-pyridin-3-yl)-methanone di-hydrochloride was isolated as a pale yellow solid. MS(EI): 414 (M⁺+H).

EXAMPLE 94

10 <u>1-[4-(5-Aminomethyl-3-hydroxyphenyl)-piperidin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone di-</u> hydrochloride

A. 3-Bromo-N,N-(bis-tert-butoxycarbonyl)-5-(tert-butyldimethylsilyloxy)benzylamine (3-Bromo-5-methyl-phenoxy)-tert-butyldimethylsilane (3.32mmol) [prepared according to the procedure of J. E. Baldwin et al, Tetrahedron, 1991, 47(29), 5603], N-bromosuccinimide (3.65mmol), and benzoyl peroxide (0.332mmol) were dissolved in dichloromethane (10mL) and the reaction mixture irradiated for 4 hours. Diluted with dichloromethane and washed with water, dried over magnesium sulfate and concentrated to dryness. The crude material was purified by column chromatography on silica gel with 10% ethyl acetate / cyclohexane to give (3-bromo-5-bromomethyl-phenoxy)-tert-butyldimethylsilane as a colorless oil. This material was subjected to the conditions described in the first part of EXAMPLE 1A, but using (3-bromo-5-bromomethyl-phenoxy)-tert-butyldimethylsilane in place of 3-bromobenzylbromide, to give 3-bromo-N,N-(bis-tert-butoxycarbonyl)-5-(tert-butyldimethylsilyloxy)benzylamine as a colorless oil. MS (EI) 516 and 518 (M⁺+H).

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<u>B.</u> 1-(5-Phenylethynylpyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6-tetrahydropyridine By proceeding in a manner similar to the method described in EXAMPLE 17B, but using 5-phenylethynylpyridine-3-carboxylic acid in place of 5-phenethylpyridine-3-carboxylic acid, there was prepared 1-(5-phenylethynylpyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6-tetrahydropyridine as a pale yellow solid. MS (EI) 415 (M⁺+H).

C. 1-{4-[3-(N,N-bis-tert-Butoxycarbonyl)aminomethyl-5-hydroxyphenyl]-3,6-dihydro-2H-pyridin-1-yl}-1-(5-phenylethynylpyridin-3-yl)methanone

By proceeding in a manner similar to the method described in EXAMPLE 17D, but using 3-bromo-N,N-(bis-tert-butoxycarbonyl)-5-(tert-butyldimethylsilyloxy)benzylamine in place of N-(tert-butoxycarbonyl)-3-bromo-4-fluorobenzylamine and 1-(5-phenylethynylpyridine-3-carbonyl)-4-

(pinacolatoboronyl)-1,2,3,6-tetrahydropyridine in place of 1-(5-phenylethylpyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6-tetrahydropyridine, there was prepared 1-{4-[3-(N,N-bis-tert-Butoxycarbonyl)aminomethyl-5-hydroxyphenyl]-3,6-dihydro-2H-pyridin-1-yl}-1-(5-phenylethynylpyridin-3-yl)methanone as a pale brown solid. MS (EI) 610 (M⁺+H). The tert-butyl-dimethylsilyl moiety had unexpectedly been removed during this procedure.

D. 1-[4-(5-Aminomethyl-3-hydroxyphenyl)-piperidin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone di-hydrochloride

By proceeding in a manner similar to the method described in EXAMPLE 2A, but using 1-{4-[3-(N,N-bis-tert-butoxycarbonyl)aminomethyl-5-hydroxyphenyl]-3,6-dihydro-2H-pyridin-1-yl}-1-(5-phenylethynylpyridin-3-yl)methanone in place of 5-phenylethynylpyridine-3-carboxylic acid, there was prepared 1-{4-[3-(N,N-bis-tert-butoxycarbonyl)aminomethyl-5-hydroxy-phenyl]piperidin-1-yl}-1-(5-phenethylpyridin-3-yl)methanone. The crude product from this reaction was purified by column chromatography on silica gel, before being subjected to the same conditions as described in EXAMPLE 1D, but using 1-{4-[3-(N,N-bis-tert-butoxycarbonyl)aminomethyl-5-hydroxy-phenyl]piperidin-1-yl}-1-(5-phenethylpyridin-3-yl)methanone in place of 3-[1-(5-phenylethynylpyridine-3-carbonyl)piperidin-4-yl]benzonitrile. 1-[4-(5-Aminomethyl-3-hydroxyphenyl)-piperidin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone di-hydrochloride was isolated as a pale yellow solid. MS(EI): 416 (M++H).

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EXAMPLE 95

1-[4-(5-Aminomethyl-2-hydroxyphenyl)-piperidin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone di-hydrochloride

A. 4-Benzyloxy-3-bromobenzyl carbamic acid tert-butyl ester

3-Bromo-4-flurobenzonitrile (3.00 g, 15 mmol), benzyl alcohol (1.71 ml, 16.5 mmol) and THF (40 ml) are combined and treated with 60 % sodium hydride in oil (0.66 g, 16.5 mmol). The reaction mixture is heated to reflux under nitrogen for 3 hours. Aqueous workup and chromatographic purification (cyclohexane:dichloromethane, 3:1) yields 4-benzyloxy-3-bromobenzonitrile as a white solid (3.88 g, 13.5 mmol). A portion of this material (2.64 g, 9.16 mmol) in THF (25 ml) is treated with a 1 M solution of borane in THF (18.3 ml, 18.3 mmol). After the exotherm subsides the reaction is refluxed a couple of days under nitrogen. The excess borane is destroyed by the addition of methanol and 4-benzyloxy-3-bromobenzylamine is precipitated as the hydrochloride salt (1.58 g, 4.8 mmol). This material is suspended in dichloromethane (30 ml) and treated successively with triethyl amine (1.68 ml, 12.02 mmol) and di-tert-butyl dicarbonate (1.26 g, 5.77 mmol). The reaction mixture is stirred under nitrogen four hours; aqueous workup and chromatographic purification (ethyl

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acetate:cyclohexane, 3:7) yields the title compound as a white solid (1.69 g, 4.3 mmol). MS(EI): 394(M⁺).

- B. 4-Benzyloxy-3-{1-[1-(5-phenylethylpyridin-3-yl)methanoyl]-1,2,3,6-tetrahydropyridin-4-yl}-benzyl carbamic acid *tert*-butyl ester
- 1-(5-Phenylethylpyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6-tetrahyropyridine (0.628 g, 1.5 mmol) as prepared in EXAMPLE 17B, 4-benzyloxy-3-bromobenzyl carbamic acid *tert*-butyl ester (0.62 g, 1.58 mmol), dichlorobis(triphenylphosphine)palladium (II) (0.074, 0.08 mmol), potassium carbonate (0.622 g, 4.5 mmol) and DMF (15 mL) are heated to 80 °C under nitrogen for 3 hours. The DMF is removed in vacuo, the residue is subjected to an aqueous workup and the organic residue is purified by chromatography to give a gray foam (0.45 g, 0.75 mmol).
- C. 3-Hydroxy-2-{1-[1-(5-phenylethylpyridin-3-yl)methanoyl]-piperidin-4-yl}-benzyl carbamic acid *tert*-butyl ester
- 4-Benzyloxy-3-{1-[1-(5-phenylethylpyridin-3-yl)methanoyl]-1,2,3,6-tetrahydropyridin-4-yl}-benzyl carbamic acid *tert*-butyl ester (0.34 g, 0.56 mmol) is hydrogenolyzed with hydrogen gas and 10% P/C to give the title compound as a white foam (0.27 g, 0.52 mmol). MS(EI): 515(M⁺).
 - D. 1-[4-(5-Aminomethyl-2-hydroxyphenyl)-piperidin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone di-hydrochloride
 - 3-Hydroxy-2-{1-[1-(5-phenylethylpyridin-3-yl)methanoyl]-piperidin-4-yl}-benzyl carbamic acid *tert*-butyl ester (0.09 g, 0.175 mmol) is converted to the title compound (0.053 g, 0.11 nmol) by the procedure described in EXAMPLE 5C. MS(EI): 416(M⁺+H).

25 EXAMPLE 96

- 1-[4-(5-Aminomethyl-2-benzyloxyphenyl)-3,6-dihydro-2H-pyridin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone di-hydrochloride
- 4-Benzyloxy-3-{1-[1-(5-phenylethylpyridin-3-yl)methanoyl]-1,2,3,6-tetrahydropyridin-4-yl}-benzyl carbamic acid *tert*-butyl ester (0.11 g, 0.184 mmol) is converted to the title compound (0.080 g, 0.15 mmol) by the procedure described in EXAMPLE 5C. MS(EI): 504(M⁺+H).

EXAMPLE 97

- 1-[4-(3-Aminomethylphenyl)-piperidin-1-yl]-1-(4-phenylethyl-phenyl)-methanone hydrochloride

 A. 4-Phenylethynylbenzoic acid.
- 4-Phenylethynylbenzaldehylde (1.01 g, 4.85 mmol) is added to a suspension of silver oxide (0.56 g, 2.43 mmol) in water (15 ml) and sodium hydroxide (0.97 g, 24.3 mmol). The reaction mixture is

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heated to 90 °C for 1.5 hours cooled and acidified. The aqueous mixture is extracted with ethyl acetate and the organic layer is concentrated. The resultant solid is partitioned between ether and 0.1 M sodium hydroxide solution. The aqueous layer is acidified and the precipitated title compound (0.55g, 2.5 mmol) is collected. M.P. 224-225 °C; MS(EI): 222(M⁺)

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B. 1-[4-(3-Aminomethylphenyl)-piperidin-1-yl]-1-(4-phenylethyl-phenyl)-methanone hydrochloride By proceeding in similar manner to the method described in EXAMPLE 1C but using 4-phenylethynyl benzoic acid, *N*,*N*-bis-(*tert*-butoxycarbonyl)-3-[1-(4-phenylethynyl-benzoyl)-piperidin-4-yl]-benzylamine was prepared. The title compound is subsequently prepared by applying in sequence the methods described in EXAMPLE 9. MS(EI): 399(M⁺+H).

EXAMPLE 98

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[2-(2-hydroxy-phenyl)-ethyl]-phenyl}-methanone hydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 10 but using *N,N*-bis-(*tert*-butoxycarbonyl)-3-{1-[3-(2-hydroxyphenyl)ethynyl-benzoyl]-piperidin-4-yl}-benzylamine, which was prepared in a similar manner to the method described in EXAMPLE 6a but using 2-iodophenol, there was prepared the title compound as a white amorphous solid. MS(EI): 415 (M+H).

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EXAMPLE 99

1-[4-(5-Aminomethyl-2-hydroxymethylphenyl)-3,6-dihydro-2H-pyridin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone

A. Acetic acid 4-(N,N-bis-tert-butoxycarbonyl)aminomethyl-2-bromobenzyl ester

2-Bromo-4-(bromomethyl)benzylbromide (2.91mmol) [prepared according to the procedure of Bridger et al, J. Med. Chem. 1995, 38(2), 366] and di-tert-butyliminodicarboxylate (2.91mmol) were dissolved in tetrahydrofuran (10mL), and sodium hydride (60% in mineral oil, 2.91mmol) added at room temperature under argon. The reaction mixture was stirred at room temperature for 4 days, quenched with saturated aqueous ammonium chloride, extracted into ethyl acetate, washed with brine, dried over magnesium sulfate, and concentrated to dryness. The crude residue was purified by column chromatography on silica gel with cyclohexane:ethyl acetate = 9:1. 3-bromo-4-bromomethyl-(N,N-bistert-butoxycarbonyl)benzylamine was isolated as a white solid. A portion of 3-bromo-4-bromomethyl-(N,N-bistert-butoxycarbonyl)benzylamine (1.88mmol) was dissolved in acetonitrile (15mL), and to this was added potassium acetate (3.7mmol) and 18-crown-6 (0.095mmol). The reaction mixture was stirred at room temperature for 16 hours, concentrated to dryness, extracted into ethyl acetate, washed with brine, dried over magnesium sulfate, and concentrated to dryness. Purification was carried out by

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column chromatography on silica gel with diethyl ether: cyclohexane = 1:1. Acetic acid 4-(N,N-bistert-butoxycarbonyl)aminomethyl-2-bromobenzyl ester was isolated as a colorless solid. MS (EI) 458 and 460 (M⁺+H).

5 B. 1-{4-[5-(N,N-bis-tert-Butoxycarbonyl)aminomethyl-2-acetoxymethylphenyl]-3,6-dihydro-2H-pyridin-1-yl}-1-(5-phenethylpyridin-3-yl)methanone

By proceeding in a manner similar to the method described in EXAMPLE 17D, but using acetic acid 4-(N,N-bis-tert-butoxycarbonyl)aminomethyl-2-bromobenzyl ester in place of N-(tert-butoxycarbonyl)-3-bromo-4-fluorobenzylamine, there was prepared 1-{4-[5-(N,N-bis-tert-butoxycarbonyl)aminomethyl-2-acetoxymethylphenyl]-3,6-dihydro-2H-pyridin-1-yl}-1-(5-phenethylpyridin-3-yl)methanone, MS (EI) 670 (M⁺+H).

C. 1-[4-(5-Aminomethyl-2-hydroxymethylphenyl)-3,6-dihydro-2H-pyridin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone

- 1-{4-[5-(N,N-bis-tert-Butoxycarbonyl)aminomethyl-2-acetoxymethylphenyl]-3,6-dihydro-2H-pyridin-1-yl}-1-(5-phenethylpyridin-3-yl)methanone (0.3mmol) was dissolved in methanol (10mL) and cooled at 0°Cwhilst adding potassium carbonate (0.1mmol). Left at room temperature for 16 hours, concentrated to dryness and used crude residue directly in the next step. By proceeding in a manner similar to the method described in EXAMPLE 1D, but using 1-{4-[5-(N,N-bis-tert-
- butoxycarbonyl)aminomethyl-2-hydroxymethylphenyl]-3,6-dihydro-2H-pyridin-1-yl}-1-(5-phenethylpyridin-3-yl)methanone in place of 3-[1-(5-phenylethynylpyridine-3-carbonyl)piperidin-4-yl]benzonitrile, there was prepared 1-[4-(5-aminomethyl-2-hydroxymethylphenyl)-3,6-dihydro-2H-pyridin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone as a pale yellow solid. MS(EI): 428 (M++H).

25 EXAMPLE 100

1-[4-(5-Aminomethyl-thiophen-2-yl)-piperidin-1-yl]-(5-phenylethyl-pyridin-3-yl)-methanone di-hydrochloride

A. 2-[N,N-Bis-(tert-butoxycarbonyl)aminomethyl]-4-bromo-thiophene

By proceeding in a similar manner to the method described in EXAMPLE 1A but using 4-bromo-2-bromomethyl-thiophene, which was simply prepared from reduction of 4-bromo-thiophene-2-carbaldehyde and subsequent bromonation of the alcohol, there was prepared the title compound.

B. 1-[4-(5-Aminomethyl-thiophen-2-yl)-piperidin-1-yl]-(5-phenylethyl-pyridin-3-yl)-methanone dihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 93 but using 2-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-4-bromo-thiophene, there was prepared the title compound as a white amorphous solid. MS(EI): 406(M+H).

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EXAMPLE 101

[4-(5-Aminomethyl-pyridin-3-yl)-piperidin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone tribydrochloride

A. 3-Bromo-5-(N,N-bis-tert-butoxycarbonyl)aminomethylpyridine

3-Bromo-5-hydroxymethylpyridine (16.1mmol) [prepared according to the procedure of Ashimori et al, Chem. Pharm. Bull. 1990, 38(9), 2446] and pyridine (32.3mmol) were dissolved in acetonitrile (32mL) and cooled to 0°C. Dibromotriphenylphosphorane (20.9mmol) added, and left reaction mixture to warm to room temperature in stoppered flask for 4 hours. The crude reaction mixture was purified by column chromatography directly on silica gel with diethyl ether:cyclohexane = 1:1. 3-Bromo-5-bromomethylpyridine was isolated as a pale brown solid. 3-Bromo-5-bromomethylpyridine (7.7mmol) and di-tert-butyliminodicarboxylate (10mmol) were dissolved in tetrahydrofuran (20mL), and sodium hydride (60% in mineral oil, 10mmol) added at room temperature under argon. The reaction mixture was stirred at room temperature for 16 hours, quenched with saturated aqueous ammonium chloride, extracted into ethyl acetate, washed with brine, dried over magnesium sulfate, and concentrated to dryness. The crude residue was purified by column chromatography on silica gel with cyclohexane:diethyl ether = 2:1. 3-bromo-5-(N,N-bis-tert-butoxycarbonyl)aminomethylpyridine was isolated as a pale yellow solid. MS (EI) 387 and 389 (M⁺+H).

B. [4-(5-Aminomethyl-pyridin-3-yl)-piperidin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone tri-hydrochloride

By proceeding in a manner similar to the method described in EXAMPLE 17D, but using 3-bromo-5-

(N,N-bis-tert-butoxycarbonyl)aminomethylpyridine in place of N-(tert-butoxycarbonyl)-3-bromo-4fluorobenzylamine and 1-(5-phenylethynylpyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6tetrahydropyridine in place of 1-(5-phenylethylpyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6tetrahydropyridine, there was prepared 1-[5-(N,N-bis-tert-butoxycarbonyl)aminomethyl-3',6'-dihydro2'H-[3,4']bipyridinyl-1'-yl]-1-(5-phenylethynylpyridin-3-yl)methanone. This material was subjected to
the same conditions as described in EXAMPLE 2A, but using 1-[5-(N,N-bis-tertbutoxycarbonyl)aminomethyl-3',6'-dihydro-2'H-[3,4']bipyridinyl-1'-yl]-1-(5-phenylethynylpyridin-3yl)methanone in place of 5-phenylethynylpyridine-3-carboxylic acid. The crude product from this
reaction was purified by column chromatography on silica gel, before being subjected to the same
conditions as described in EXAMPLE 1D, but using {4-[5-(N,N-bis-tertbutoxycarbonyl)aminomethylpyridin-3-yl]-piperidin-1-yl}-1-(5-phenylethyl-pyridin-3-yl)-methanone

in place of 3-[1-(5-phenylethynylpyridine-3-carbonyl)piperidin-4-yl]benzonitrile. [4-(5-Aminomethyl-

pyridin-3-yl)-piperidin-1-yl]-1-(5-phenylethyl-pyridin-3-yl)-methanone tri-hydrochloride was isolated as a pale yellow solid. MS(EI): 401 (M⁺+H).

EXAMPLE 102

5 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(1-ethyl-1H-indol-3-yl)-methanone-trifluoroacetate.

A. 1-Ethyl-1H-indole-3-carboxylic acid methyl ester.

A flask was charged with 1H-indole-3-carboxylic acid methyl ester (2g, 11.41 mmol) and iodoethane (4.4g, 28.5 mmol) in dry THF (25 mL). The mixture was stirred in a water bath and a 60% dispersion of sodium hydride (0.68g, 17.12 mmol) in mineral oil was added in portions over 5 minutes. The reaction stirred for 48 hours and was quenched by careful addition of water. The mixture was extracted with dichloromethane (2 X 100 mL), dried over sodium sulfate and evaporated under reduced pressure. The crude product was purified by silica flash chromatography (10% ethyl acetate/heptane) to give 1-ethyl-1H-indole-3-carboxylic acid methyl ester (1.8g). ¹H NMR [CDCl₃]: δ 8.22-8.15 (m, 1H), 7.87 (s, 1H), 7.42-7.33 (m, 1H), 7.31-7.25 (m, 2H), 4.22 (q, 2H), 3.92 (s, 3H), 1.52 (t, 3H).

B. 1-Ethyl-1H-indole-3-carboxylic acid.

A solution of 1-ethyl-1H-indole-3-carboxylic acid methyl ester (1.8g, 8.8 mmol) was stirred in a 1:1 mixture of THF:MeOH (40mL), and to this was added 2N NaOH (20 mL). The reaction was heated at reflux for 4 hours. The reaction mixture was partially evaporated to remove the THF, MeOH and the remaining material diluted with water (20 mL) and acidified to pH=2 with 1N HCl. The mixture was extracted with dichloromethane (100 mL), dried over sodium sulfate and evaporated under reduced pressure to give the title compound as a white solid, which was used directly in the next step.

25 <u>C. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(1-ethyl-1H-indol-3-yl)-methanone-trifluoroacetate.</u>

By proceeding in a similar manner to the method described in EXAMPLE 38, but using 1-ethyl-1H-indole-3-carboxylic acid, there was prepared the title compound as an amorphous white solid. 1 H NMR [CD₃OD]: δ 7.75-7.63 (m, 2H), 7.52 (d, 1H), 7.43-7.36 (m, 3H), 7.35-7.15 (m, 3H), 4.63-4.51 (m, 2H), 4.30 (q, 2H), 4.11 (s, 2H), 3.30-3.13 (m, 2H), 3.03-2.85 (m, 1H), 2.00-1.86 (m, 2H), 1.85-1.68 (m, 2H), 1.49 (t, 3H). MS (ion spray): 362 (M⁺+1).

A. 4-Hydroxy-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester

To a solution of ethyl 4-piperidone-3-carboxylate hydrochloride (5g, 24.05mmol) in THF (70mL) and water (35mL) at 0°C, was added triethylamine (8.7mL, 62.5 mmol), followed by N-(benzyloxycarbonyloxy)succinimide (7.79g, 31.27mmol). The reaction mixture was stirred and

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allowed to warm to room temperature. After 3 hours the reaction mixture was diluted with water (50mL) and ethyl acetate (100mL) added. The aqueous phase was extracted into ethyl acetate (2x100mL). The organic phases were combined, washed with brine (50mL), dried (MgSO₄), and the solvent removed in vacuo. The crude product was purified by column chromatography on silica gel (eluent, ethyl acetate: pentane = 1:5) to give 4-hydroxy-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester as a colorless oil (7.26g, 94%). MS (EI) 305 (M⁺).

B. 4-Trifluoromethanesulfonyloxy-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester

4-Hydroxy-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester (15.94g, 52.5mmol) was dissolved in anhydrous THF (150mL) under nitrogen and cooled at -78°C during the addition of sodium bis(trimethylsilyl)amide (1M in THF; 68mL, 68mmol) via cannula. After stirring for 30 minutes at this temperature a solution of N-phenyltrifluoromethanesulfonimide (22.42g, 62.8mmol) in THF (230mL) was added dropwise via cannula. The reaction mixture was stirred at this temperature for 10 minutes before warming to 0°C and stirring for 2 hours. After 48h the reaction mixture was quenched with water, extracted into DCM, dried (MgSO₄) and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (eluent; ethyl acetate:pentane = 4:1) to give 4-trifluoromethanesulfonyloxy-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester as colorless oil (18.59g, 81%). This material decomposed to a deep red material upon standing so was stored under nitrogen at 0°C in the dark. MS (EI) 437 (M⁺).

C. 4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester

4-Trifluoromethanesulfonyloxy-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester (200mg, 0.458mmol) was dissolved in anhydrous dioxane (6mL), and added dropwise, via cannula, to a mixture of potassium acetate (135mg, 1.374mmol), 1,1'-bis(diphenylphosphino)ferrocene (8mg, 0.014mmol), [1,1'-bis(diphenylphosphino)ferroceno]dichloropalladium-dichloromethane complex (10mg, 0.014mmol), and bis-pinnacolato diborane (116mg, 0.458mmol), under nitrogen. The mixture was heated at 80°C overnight, cooled to room temperature and partitioned between DCM and water. The aqueous phase was extracted with DCM, and the organic phases combined and dried (MgSO₄). Th crude product was purified by flash column chromatography on silica gel (eluent; pentane:ethyl acetate = 5:1) to afford 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester as a colorless oil (94mg, 50%). MS (EI) 415 (M⁺).

D. 4-{3-[(N,N-Bis-tert-butoxycarbonyl)aminomethyl]phenyl}-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester

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A solution of 3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]bromobenzene (3.51g, 9.1mmol) [prepared by the method in Example 1A] and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester (3.6g, 8.67mmol) in DMF (120mL) were added, via cannula, to a mixture of [1,1'-

bis(diphenylphosphino)ferroceno]dichloropalladium-dichloromethane complex (425mg, 0.52mmol) and potassium carbonate (3.59g, 26mmol) under nitrogen. The reaction mixture was heated at 80°C overnight, concentrated to dryness in vacuo, and the residue partitioned between DCM and water. The aqueous phase was extracted with DCM, the organic phases combined, washed with brine, and dried (MgSO₄). The crude material was purified by column chromatography on silica gel (eluent; pentane:
 ethyl acetate = 6:1) to give 4-{3-[(N,N-bis-tert-butoxycarbonyl)aminomethyl]phenyl}-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester as a colorless oil (2.27g, 44%). MS (EI) 594 (M⁺).

E. (3S, 4S) and (3R,4R) 4-{3-[(N,N-Bis-tert-butoxycarbonyl)aminomethyl]phenyl}-piperidine-3-carboxylic acid ethyl ester

Solid carbon dioxide (1g) was added to a solution of 4-{3-[(N,N-bis-tert-butoxycarbonyl)aminomethyl]phenyl}-5,6-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester (2.07g, 3.48mmol) in IMS (20mL). 10% palladium on carbon (200mg) was added and the reaction mixture stirred at room temperature, under an atmosphere of hydrogen, for 4 hours. The palladium on carbon was filtered off through celite to give a 1:1 mixture of (3S, 4S) and (3R,4R) 4-{3-[(N,N-Bis-tert-butoxycarbonyl)aminomethyl]phenyl}-piperidine-3-carboxylic acid ethyl ester as a pale grey/brown oil (1.35g, 84%), which was pure enough for use in the subsequent reaction. MS (EI) 462 (M⁺).

F. (3S,4S) and (3R,4R)-4-{3-[(Bis-tert-butoxycarbonyl)aminomethyl]phenyl}-1-(5-phenethylpyridine-3-carbonyl)piperidine-3-carboxylic acid ethyl ester

By proceeding in a similar manner to the method described in EXAMPLE 2B, but using a 1:1 mixture of (3S, 4S) and (3R,4R) 4-{3-[(N,N-Bis-tert-butoxycarbonyl)aminomethyl]phenyl}-piperidine-3-carboxylic acid ethyl ester instead of 4-{3-[N,N-bis(tert-

butoxycarbonyl)aminomethyl]phenyl}piperidine, there was prepared a 1:1 mixture of (3S,4S) and (3R,4R)-4-{3-[(Bis-tert-butoxycarbonyl)aminomethyl]phenyl}-1-(5-phenethylpyridine-3-carbonyl)piperidine-3-carboxylic acid ethyl ester as a colorless glassy solid (414mg, 0.62mmol). MS (EI) 671 (M[†]).

35 G. (3S,4S) and (3R, 4R)-4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester dihydrochloride

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By proceeding in a similar manner to the method described in EXAMPLE 1D, but using a 1:1 mixture of (3S,4S) and (3R,4R)-4-{3-[(Bis-tert-butoxycarbonyl)aminomethyl]phenyl}-1-(5-phenethylpyridine-3-carbonyl)piperidine-3-carboxylic acid ethyl ester instead of N,N-bis-(tert-butoxycarbonyl)-3-[1-(5-phenylethynylpyridine-3-carbonyl)piperidin-4-yl]benzylamine, there was prepared a 1:1 mixture of (3S,4S) and (3R, 4R)-4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester dihydrochloride as a white solid. MS (EI) 471 (M⁺).

EXAMPLE 104

(3R,4S) and (3S, 4R)-4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester dihydrochloride

A. (3R,4S) and (3S,4R)-4-{3-[(tert-Butoxycarbonyl)aminomethyl]phenyl}-1-(5-phenethylpyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester

Sodium hydride (10mg, 60% in mineral oil, 0.25mmol) was added to ethanol (10mL), and after the effervescence had subsided a 1:1 mixture of (3S,4S) and (3R,4R)-4-{3-[(bis-tert-butoxycarbonyl)aminomethyl]phenyl}-1-(5-phenethylpyridine-3-carbonyl)piperidine-3-carboxylic acid ethyl ester (100mg) was added at room temperature. After 1 hour the solvent was removed in vacuo, and the residue partitioned between DCM and water. The aqueous phase was extracted with DCM, the combined organic phase washed with brine and dried (MgSO₄). The crude material was purified by column chromatography on silica gel (eluent; DCM:MeOH = 10:1) to give a 1:1 mixture of (3R,4S) and (3S,4R)-4-{3-[(tert-butoxycarbonyl)aminomethyl]phenyl}-1-(5-phenethylpyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester as a pale yellow glassy solid (43mg, 51%). MS (EI) 571 (M⁺).

B. (3R,4S) and (3S, 4R)-4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester dihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 1D, but using a 1:1 mixture of (3R,4S) and (3S,4R)-4-{3-[(tert-butoxycarbonyl)aminomethyl]phenyl}-1-(5-phenethylpyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester instead of N,N-bis-(tert-butoxycarbonyl)-3-[1-(5-phenylethynylpyridine-3-carbonyl)piperidin-4-yl]benzylamine, there was prepared a 1:1 mixture of (3R,4S) and (3S, 4R)-4-(3-aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester dihydrochloride as a white solid. MS (EI) 471 (M⁺).

EXAMPLE 105

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(4-bromo-2-fluoro-benzylamino)-pyridin-3-yl]-methanone trihydrochloride

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A. 5-tert-Butoxycarbonylamino-nicotinic acid

To a solution of diethyl 3,5-pyridinedicarboxylate [prepared according to the procedure of J. C. Speelman and R. M. Kellogg, J. Org. Chem., 1990, 55 (2), pages 647-653; 64.19 g, 0.248 mol] in ethanol (650 mL) were added KOH pellets (14.56 g, 0.260 mol). The reaction mixture was stirred overnight at ambient temperature. Evaporation of solvent afforded a white solid that was rinsed with dichloromethane, and then dissolved in water. The aqueous solution was extracted with ether, and then acidified to pH 3. The resultant white precipitate was collected by filtration and dried to afford pyridine-3,5-dicarboxylic acid monomethyl ester (33.70 g). A portion of this material (10.00 g, 51.3 mmol) was dissolved in dry tert-butanol (300 mL) and treated sequentially with triethylamine (7.85 mL, 56.4 mmol) and diphenyl phosphoryl azide (11.5 mL, 53.4 mmol). The mixture was refluxed for 90 minutes, and then stirred at ambient temperature overnight. Solvent was removed under reduced pressure and the residue was partitioned between water and dichloromethane. The layers were separated and the aqueous phase was extracted twice with dichloromethane. The combined organic phases were dried and concentrated. Chromatography on silica gel eluting with a mixture of pentane and ethyl acetate (3:1, v/v) gave 5-tert-butoxycarbonylamino-nicotinic acid ethyl ester (4.79 g). This ester was dissolved in methanol (45 mL) and treated with 1 N NaOH (54 mL, 54 mmol). After stirring 2 hours, volatiles were evaporated under reduced pressure and the residue was treated with 1 N HCl until the resultant slurry reached pH 3. The precipitate was collected by filtration, washed with water, and dried to afford 5-tert-butoxycarbonylamino-nicotinic acid (4.21 g): ¹H NMR (300 MHz, DMSOd₆) δ 13.39 (br s, 1H), 9.82 (s, 1H), 8.78 (d, J=2.5 Hz, 1H), 8.69 (d, J=1.9 Hz, 1H), 8.45-8.50 (m, 1H), 1.50 (s, 9H); ¹³C NMR (75 MHz, DMSO-d₆) δ 166.2, 152.7, 143.4, 143.2, 136.2, 126.3, 124.9, 80.0, 27.9; MS (ESI) m/z 239 (M+H).

B. {5-[1-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)methanoyl]-pyridin-3-yl}carbamic acid tert-butyl ester

To a 0 °C solution of 4-{3-[*N,N*-bis-(*tert*-butoxycarbonyl)aminomethyl]-phenyl}-piperidine (0.1545 g, 0.3956 mmol, EXAMPLE 1B), 5-*tert*-butoxycarbonylamino-nicotinic acid (0.0966 g, 0.4055 mmol), 1-hydroxy-7-azabenzotriazole (0.0290 g, 0.2131 mmol), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.1500 g, 0.7824 mmol) in dimethylformamide (5.0 mL) was added pyridine (0.065 mL, 0.8037 mmol). The reaction mixture was stirred 30 minutes at 0 °C, then allowed to warm to room temperature under inert atmosphere. After 16 hours at ambient temperature the reaction solution was diluted with ethyl acetate (30 mL), washed with saturated ammonium chloride (2 x 15 mL), saturated sodium bicarbonate (15 mL), and brine (15 mL). The organic phase was dried over magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by silica gel chromatography eluting with a mixture of ethyl acetate and methylene chloride (1:1, v/v) to give {5-[1-

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 $\frac{(4-\{3-[N,N-\text{bis-}(\textit{tert-}\text{butoxycarbonyl})\text{aminomethyl}]-\text{phenyl}\}-\text{piperidin-}1-\text{yl})\text{methanoyl}]-\text{pyridin-}3-\text{yl}\text{carbamic acid }\textit{tert-}\text{butyl ester}} \text{ as a colorless oil } (0.1812 \text{ g}): TLC, 50:50-\text{methylene chloride:ethyl} acetate, $R_f=0.20.$ 1H NMR (300 MHz, CDCl_3) $\delta 8.67 (d, J=2.6 Hz, 1H), 8.34 (d, J=1.4 Hz, 1H), 8.09 (s, 1H), 7.93 (s, 1H), 7.21-7.35 (m, 1H), 7.08-7.18 (m, 3H), 4.81-4.93 (m, 1H), 4.78 (s, 2H), 3.81-3.93 (br m, 1H), 3.11-3.28 (br m, 1H), 2.70-2.96 (m, 2H), 1.51 (s, 9H), 1.45 (s, 18H), 1.40-2.02 (m partially obscured, 4H); 13C NMR (75 MHz, CDCl_3) $\delta 167.5, 152.6, 152.5, 144.8, 141.3, 141.0, 138.9, 135.7, 131.8, 128.5, 125.6, 125.3, 125.2, 124.1, 82.4, 81.0, 77.2, 49.3, 42.5, 28.1, 27.8; MS (CI) m/z 611 (M+H). 13C NMR (75 MHz, CDCl_3) $\delta 1.0, 77.2, 49.3, 42.5, 28.1, 27.8; MS (CI) m/z 611 (M+H). 13C NMR (75 MHz, CDCl_3) $\delta 1.0, 77.2, 49.3, 42.5, 28.1, 27.8; MS (CI) m/z 611 (M+H).$

- 10 C. (4-Bromo-2-fluoro-benzyl)-{5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}piperidin-1-yl)-methanoyl]-pyridin-3-yl}-carbamic acid dimethyl-ethyl ester To a solution of {5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-lyl)methanoyl]-pyridin-3-yl}carbamic acid tert-butyl ester (0.0745 g, 0.1220 mmol) in dimethylformamide (2.0 mL) was added sodium hydride (61% suspension in mineral oil, 0.0216 g, 15 0.5499 mmol). Deprotonation was allowed to occur over 3 minutes while stirring under inert atmosphere. 4-Bromo-2-fluorobenzyl bromide (0.1559 g,0.5819 mmol) was added to the anion solution. The mixture was stirred an additional 10 minutes, then quenched with water (5.0 mL). The reaction solution was extracted with ethyl acetate (15 mL), and the organic phase was washed with brine (2 x 10 mL), dried over magnesium sulfate, filtered, and evaporated to dryness. Purification of the residue on silica gel eluting first with ethyl acetate/methylene chloride/hexane (1:1:2, v/v/v) and 20 then with ethyl acetate and methylene chloride (1:1, v/v) afforded (4-bromo-2-fluoro-benzyl)-{5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}carbamic acid dimethyl-ethyl ester as a colorless oil (0.0917 g): TLC, 50:50-methylene chloride:ethyl acetate, $R_f = 0.59$. ¹H NMR (300 MHz, CDCl₃) δ 8.47-8.51 (m, 2H), 7.61 (br s, 1H), 7.07-7.32 (m, 7H), 4.89 (s, 2H), 4.78 (s, 2H), 4.77-4.92 (m partially obscured, 1H), 3.68-3.83 (br m, 1H), 3.09-3.24 25 (br m, 1H), 2.70-2.97 (m, 2H), 1.45 (s, 18H), 1.44 (s, 9H), 1.30-2.04 (m partially obscured, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 167.0, 160.4 (d, 250.8), 154.0, 152.7, 148.5, 144.9, 139.0, 138.7, 132.2, 131.9, 130.7, 129.7, 127.9 (d, 3.4), 125.8, 125.7, 125.3, 123.8 (d, 14.5), 121.8 (d, 9.7), 119.3 (d, 24.8), 82.5, 82.2, 49.5, 46.9, 42.6, 32.8 (br), 28.4, 28.2, 28.0; ¹⁹F NMR (282 MHz, CDCl₃) δ -114.9; MS (CI) m/z 797 (M+H). 30
 - D. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(4-bromo-2-fluoro-benzylamino)-pyridin-3-yl]-methanone trihydrochloride

 (4-Bromo-2-fluoro-benzyl)-{5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-

piperidin-1-yl)-methanoyl]-pyridin-3-yl}-carbamic acid dimethyl-ethyl ester (0.0806 g, 0.1010 mmol)

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was treated with 4 *M* HCl in 1,4-dioxane (2.0 mL, 8.0 mmol) and stirred at ambient temperature. After 25 minutes the reaction mixture was diluted with isopropyl alcohol (0.5 mL) and stirring was continued for an additional 2.5 hours. Dripping the reaction solution into ether (40 mL) with vigorous stirring afforded a white precipitate which was collected by filtration, washed with fresh ether (3.0 mL), and dried to afford 1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(4-bromo-2-fluoro-benzylamino)-pyridin-3-yl]-methanone trihydrochloride (0.0563 g): ¹H NMR (300 MHz, DMSO-d6) δ 8.39 (br s, 2H), 8.16 (d, J=2.7 Hz, 1H), 8.08 (s, 1H), 7.16-7.70 (m, 8H), 4.49-4.64 (br m, 1H), 4.46 (s, 2H), 4.05-4.30 (m, 1H), 4.00 (AB q, J=5.7 Hz, 2H), 3.01-3.25 (m, 1H), 2.77-2.95 (m, 2H), 1.75-1.92 (m, 1H), 1.45-1.75 (br m, 3H); ¹⁹F NMR (282 MHz, DMSO-d6) δ -114.1; MS (ESI) m/z 497 (M+H).

EXAMPLE 106

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-benzylamino-pyridin-3-yl)-methanone trihydrochloride

A. Benzyl-{5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)-

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methanoyl]-pyridin-3-yl}-carbamic acid dimethyl-ethyl ester By proceeding in a similar manner to the method described in EXAMPLE 105C, but using benzyl bromide in place of 4-bromo-2-fluorobenzyl bromide, there was prepared benzyl-{5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-carbamic acid dimethyl-ethyl ester as a yellow oil. TLC, 50:50-methylene chloride:ethyl acetate, R_f = 0.48. 1 H NMR (300 MHz, CDCl₃) δ 8.52 (d, J=2.2 Hz, 1H), 8.46 (d, J=1.2 Hz, 1H), 7.56 (s, 1H), 7.04-7.38 (m, 9H), 4.89 (s, 2H), 4.78 (s, 2H), 4.75-4.90 (m partially obscured, 1H), 3.63-3.88 (br m, 1H), 3.00-3.19 (br m, 1H), 2.68-2.90 (m, 2H), 1.45 (s, 18H), 1.44 (s, 9H), 1.37-2.04 (m, 4H); 13 C NMR (75 MHz, CDCl₃) δ 167.0, 154.1, 152.6, 148.4, 144.8, 144.5, 138.9, 137.5, 132.0, 131.5, 128.6, 128.5, 127.5, 127.2, 125.7, 125.5, 125.2, 82.4, 81.6, 53.4, 49.4, 42.5, 33.8, 28.3, 28.1, 27.9; MS (CI) m/z 701 (M+H).

B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-benzylamino-pyridin-3-yl)-methanone trihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using benzyl-{5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-carbamic acid dimethyl-ethyl ester, there was prepared 1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-(5-benzylamino-pyridin-3-yl)-methanone trihydrochloride as a white solid. ¹H NMR (300 MHz, DMSO-d6) δ 8.45 (br s, 2H), 8.13 (d, J=2.5 Hz, 1H), 8.08 (d, J=1.0 Hz, 1H), 7.54 (s, 1H), 7.47 (s, 1H), 7.18-7.45 (m, 8H), 4.50-4.63 (br m, 1H), 4.45 (s, 2H), 4.02-4.12 (m, 1H), 3.99 (AB q, J=5.5 Hz, 2H),

3.05-3.25 (m, 1H), 2.70-2.95 (m, 2H), 1.75-1.90 (br m, 1H), 1.50-1.70 (br m, 3H); MS (ESI) m/z 401 (M+H).

EXAMPLE 107

- 5 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{5-[(naphthalen-2-ylmethyl)-amino]-pyridin-3-yl}-</u> methanone trihydrochloride
 - A. {5-[1-(4-{3-[*N,N*-Bis-(*tert*-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)-methanoyl}-pyridin-3-yl}-naphthalen-2-ylmethyl-carbamic acid dimethyl-ethyl ester
- By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 2- (bromomethyl)naphthalene in place of 4-bromo-2-fluorobenzyl bromide, there was prepared {5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)-methanoyl}-pyridin-3-yl}-naphthalen-2-ylmethyl-carbamic acid dimethyl-ethyl ester as a colorless oil. TLC, 50:50-methylene chloride:ethyl acetate, R_f = 0.42. ¹H NMR (300 MHz, CDCl₃) δ 8.55 (d, J=1.8 Hz, 1H), 8.13 (d,
- J=187.5 Hz, 1H), 7.68-7.83 (m, 3H), 7.60 (s, 1H), 7.54 (br s, 1H), 7.35-7.49 (m, 3H), 7.21-7.29 (m partially obscured, 1H), 7.16 (d, J=7.7 Hz, 1H), 7.08 (s, 1H), 7.01 (d, J=7.7 Hz, 1H), 5.00-5.08 (m, 2H), 4.77 (s, 2H), 3.48-3.62 (br m, 1H), 2.59-3.03 (m, 3H), 1.45 (s, 27H), 1.27-1.95 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 166.9, 154.3, 152.6, 148.6, 144.8, 144.7, 138.9, 138.8, 134.9, 133.3, 132.8, 132.2, 131.6, 128.6, 127.7, 126.3, 126.2, 126.0, 125.8, 125.5, 125.3, 125.2, 82.4, 81.8, 53.6, 49.4, 42.5, 33.2, 28.4, 28.2, 28.0; MS (CI) m/z 752 (M+H).
 - B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{5-[(naphthalen-2-ylmethyl)-amino]-pyridin-3-yl}-methanone trihydrochloride
- By proceeding in a similar manner to the method described in EXAMPLE 105D, but using {5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)-methanoyl}-pyridin-3-yl}-naphthalen-2-ylmethyl-carbamic acid dimethyl-ethyl ester, there was prepared 1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-{5-[(naphthalen-2-ylmethyl)-amino]-pyridin-3-yl}-methanone

 trihydrochloride as a as a white solid. ¹H NMR (300 MHz, DMSO-d6) δ 8.34 (br s, 2H), 8.17 (s, 1H), 8.03 (s, 1H), 7.75-7.97 (m, 4H), 5.58-7.77 (m, 1H), 7.25-7.57 (m, 6H), 7.22 (d, J=7.2 Hz, 1H), 4.61 (s, 2H), 4.50-4.68 (m partially obscured, 1H), 4.10-4.35 (m, 1H), 4.00 (AB q, J=5.7 Hz, 2H), 2.91-3.12 (m, 1H), 2.66-2.90 (m, 2H), 1.70-1.89 (m, 1H), 1.36-1.69 (m, 3H); MS (ESI) m/z 451 (M+H).

EXAMPLE 108

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(4-bromo-benzylamino)-pyridin-3-yl]-methanone trihydrochloride

A. (4-Bromobenzyl)-{5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-carbamic acid dimethyl-ethyl ester
By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 4-bromobenzyl bromide in place of 4-bromo-2-fluorobenzyl bromide, there was prepared (4-bromobenzyl)-{5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-carbamic acid dimethyl-ethyl ester as a colorless oil. TLC, 50:50-methylene chloride:ethyl acetate, R_f = 0.41. ¹H NMR (300 MHz, CDCl₃) δ 8.45-8.51 (m, 2H), 7.56 (br s, 1H), 7.43 (d, J=8.4 Hz, 2H), 7.24-7.30 (m partially obscured, 1H), 7.11 (d, J=8.4 Hz, 2H), 6.96-7.17 (m partially obscured, 3H), 4.83 (s, 2H), 4.77 (s, 2H), 4.75-4.87 (m partially obscured, 1H), 3.65-3.80 (br m, 1H), 3.05-3.23 (br m, 1H), 2.69-2.91 (m, 2H), 1.45 (s, 18H), 1.43 (s, 9H), 1.30-2.00 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 166.8, 154.0, 152.5, 148.4, 144.7, 138.9, 138.7, 136.5, 132.1, 131.8, 131.7, 131.5, 129.0, 128.6, 125.7, 125.5, 125.2, 121.4, 82.4, 81.9, 52.8, 49.3, 42.5, 33.5, 28.3, 28.1, 27.9; MS (CI) m/z 781 (M+H).

B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(4-bromo-benzylamino)-pyridin-3-yl]-methanone trihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using (4-bromobenzyl)-{5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-carbamic acid dimethyl-ethyl ester, there was prepared 1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(4-bromo-benzylamino)-pyridin-3-yl]-methanone trihydrochloride as a cream-colored solid. ¹H NMR (300 MHz, DMSO-d6) δ 8.34 (br s, 2H), 8.11 (d, J=2.5 Hz, 1H), 8.04 (s, 1H), 7.52 (d, J=8.5 Hz, 2H), 7.34 (d, J=8.5 Hz, 2H), 7.15-7.67 (m, 5H), 4.49-4.64 (br m, 1H), 4.42 (s, 2H), 4.05-4.15 (m, 1H), 4.01 (AB q, J=5.7 Hz, 2H), 3.00-3.20 (m, 1H), 2.70-2.90 (m, 2H), 1.72-1.88 (m, 1H), 1.45-1.70 (m, 3H); MS (ESI) m/z 479 (M+H).

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EXAMPLE 109

3-[(5-{1-[4-(3-Aminomethyl-phenyl)piperidin-1-yl]-methanoyl}-pyridin-3-ylamino)-methyl]-benzonitrile trihydrochloride

A. {5-[1-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]pyridin-3-yl}-(3-cyano-benzyl)-carbamic acid dimethyl-ethyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but α-bromo-mtolunitrile in place of 4-bromo-2-fluorobenzyl bromide, there was prepared {5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-(3-cyano-benzyl)carbamic acid dimethyl-ethyl ester as a yellow oil. TLC, 50:50-methylene chloride:ethyl acetate, Rf =

0.44. ¹H NMR (300 MHz, CDCl₃) δ 8.46-8.52 (m, 2H), 7.51-7.65 (m, 3H), 7.36-7.50 (m, 2H), 7.24-7.31 (m partially obscured, 1H), 7.03-7.18 (m, 3H), 4.92 (s, 2H), 4.79-4.92 (m partially obscured, 1H), 4.78 (s, 2H), 3.70-3.85 (br m, 1H), 3.10-3.28 (br m, 1H), 2.71-2.99 (m, 2H), 1.45 (s, 18H), 1.44 (s, 9H), 1.30-2.05 (m partially obscured, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 166.7, 153.8, 152.5, 148.1, 145.2, 144.7, 139.2, 138.9, 138.7, 132.1, 131.9, 131.5, 131.2, 130.6, 129.6, 128.6, 125.6, 125.5, 125.2, 118.3, 112.9, 82.4, 80.6, 52.8, 49.3, 42.4, 33.5, 28.3, 28.0, 27.9; MS (CI) m/z 727 (M+H).

B. 3-[(5-{1-[4-(3-Aminomethyl-phenyl)piperidin-1-yl]-methanoyl}-pyridin-3-ylamino)-methyl]-benzonitrile trihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using {5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-(3-cyano-benzyl)-carbamic acid dimethyl-ethyl ester, there was prepared 3-[(5-{1-[4-(3-aminomethyl-phenyl)piperidin-1-yl]-methanoyl}-pyridin-3-ylamino)-methyl]-benzonitrile trihydrochloride as a white solid. ¹H NMR (300 MHz, DMSO-d6) δ 8.33 (br s, 2H), 8.13 (d, J=2.5 Hz, 1H), 8.02 (s, 1H), 7.80-7.91 (m, 1H), 7.63-7.75 (m, 2H), 7.42-7.58 (m, 2H), 7.20-7.7.41 (m, 4H), 4.51 (s, 2H), 4.40-4.62 (m partially obscured, 1H), 4.10-4.25 (m, 1H), 4.00 (AB q, J=5.7 Hz, 2H), 2.90-3.20 (m, 1H), 2.72-2.93 (m, 2H), 1.75-1.90 (br m, 1H), 1.45-1.70 (br m, 3H); MS (ESI) m/z 426 (M+H).

EXAMPLE 110

20 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(2-chloro-4-fluoro-benzylamino)-pyridin-3-yl]-methanone trihydrochloride</u>

A. {5-[1-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-(2-chloro-4-fluoro-benzyl)-carbamic acid dimethyl-ethyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 2-chloro-4-fluorobenzyl bromide in place of 4-bromo-2-fluorobenzyl bromide, there was prepared {5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-(2-chloro-4-fluoro-benzyl)-carbamic acid dimethyl-ethyl ester as a colorless oil. TLC, 50:50-methylene chloride:ethyl acetate, R_f = 0.48. ¹H NMR (300 MHz, CDCl₃) δ 8.51 (d, J=2.2 Hz, 1H), 8.46 (d, J=1.8 Hz, 1H), 7.62 (s, 1H), 7.24-7.34 (m, 2H), 7.04-7.19 (m, 4H), 6.97 (td, J=8.2, 2.5 Hz, 1H), 4.96 (s, 2H), 4.77 (s, 2H), 4.75-4.90 (m partially obscured, 1H), 3.70-3.85 (br m, 1H), 3.05-3.25 (br m, 1H), 2.70-2.90 (m, J=21.45, s Hz, 18H), 1.44 (s, 9H), 1.30-2.05 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 166.9, 161.8 (d, 250.1), 153.8, 152.6, 148.1, 144.7, 144.6, 138.9, 138.6, 133.6 (d, 9.7), 131.8, 131.7, 130.8 (d, 3.4), 129.8 (d, 7.6), 128.6, 125.7, 125.6, 125.2, 117.0 (d, 24.9), 114.3 (d, 21.4), 82.4, 82.1, 50.3, 49.4, 42.5, 33.8, 28.3, 28.1, 27.9; ¹⁹F NMR (282 MHz, CDCl₃) δ -112.0; MS (CI) m/z 754 (M+H).

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B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(2-chloro-4-fluoro-benzylamino)-pyridin-3-yl]-methanone trihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using {5-[1-(4-{3-[*N,N*-bis-(*tert*-butoxycarbonyl)aminomethyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-(2-chloro-4-fluoro-benzyl)-carbamic acid dimethyl-ethyl ester, there was prepared 1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(2-chloro-4-fluoro-benzylamino)-pyridin-3-yl]-methanone trihydrochloride as a white solid. ¹H NMR (300 MHz, DMSO-d6) δ 8.34 (br s, 2H), 8.15 (d, J=2.5 Hz, 1H), 8.07 (s, 1H), 7.12-7.55 (m, 8H), 4.50-4.65 (br m, 1H), 4.46 (s, 2H), 4.12-4.24 (br m, 1H), 4.00 (AB q, J=5.8 Hz, 2H), 3.05-3.20 (br m, 1H), 2.70-2.90 (m, 2H), 1.72-1.90 (br m, 1H), 1.48-1.73 (br m, 3H); ¹⁹F NMR (282 MHz, DMSO-d6) δ -112.6; MS (ESI) m/z 453 (M+H).

EXAMPLE 111

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(4-trifluoromethoxy-benzylamino)-pyridin-3-yl]-methanone trihydrochloride

A. {5-[1-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-(4-trifluoromethoxy-benzyl)-carbamic acid dimethyl-ethyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 4(trifluoromethoxy)benzyl bromide in place of 4-bromo-2-fluorobenzyl bromide, there was prepared
{5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]pyridin-3-yl}-(4-trifluoromethoxy-benzyl)-carbamic acid dimethyl-ethyl ester as a colorless oil. TLC,
50:50-methylene chloride:ethyl acetate, R_f = 0.48. ¹H NMR (300 MHz, CDCl₃) δ 8.45-8.53 (m, 2H),
7.60 (s, 1H), 7.20-7.30 (m, 3H), 7.05-7.20 (m, 5H), 4.88 (s, 2H), 4.77 (s, 2H), 4.75-4.90 (m partially
obscured, 1H), 3.70-3.84 (br m, 1H), 3.08-3.24 (br m, 1H), 2.70-2.93 (m, 2H), 1.45 (s, 18H), 1.44 (s,
9H), 1.35-2.05 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 166.9, 154.0, 152.6, 148.3, 144.7, 144.6,
138.9, 138.8, 136.3, 132.2, 131.9, 128.7, 128.6, 125.7, 125.6, 125.2, 121.2, 120.1 (q, 262), 82.4, 82.0,
52.7, 49.4, 42.5, 32.3, 28.3, 28.1, 27.9; ¹⁹F NMR (282 MHz, CDCl₃) δ -57.4; MS (CI) m/z 786
(M+H).

B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(4-trifluoromethoxy-benzylamino)-pyridin-3-yl]-methanone trihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using {5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-(4-trifluoromethoxy-benzyl)-carbamic acid dimethyl-ethyl ester, there was prepared 1-[4-(3-

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aminomethyl-phenyl)-piperidin-1-yl]-1-[5-(4-trifluoromethoxy-benzylamino)-pyridin-3-yl]-methanone trihydrochloride as a white solid. 1 H NMR (300 MHz, DMSO-d₆) δ 8.35 (br s, 2H), 8.12 (d, J=2.8 Hz, 1H), 8.05 (s, 1H), 7.20-7.75 (m, 9H), 4.50-4.65 (m, 1H), 4.48 (s, 2H), 4.05-4.20 (m, 1H), 4.00 (AB q, J=5.9 Hz, 2H), 3.05-3.25 (m, 1H), 2.70-2.90 (m, 2H), 1.75-1.90 (m, 1H), 1.50-1.70 (br m, 3H); 19 F NMR (282 MHz, DMSO-d₆) δ -56.3; MS (ESI) m/z 485 (M+H).

EXAMPLE 112

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{5-[(pyridin-3-ylmethyl)-amino]-pyridin-3-yl}-methanone tetrahydrochloride

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A. $\{5-[1-(4-\{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl\}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-pyridin-3-ylmethyl-carbamic acid dimethyl-ethyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 3-(chloromethyl)pyridine hydrochloride in place of 4-bromo-2-fluorobenzyl bromide, there was prepared <math>\{5-[1-(4-\{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl\}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-pyridin-3-ylmethyl-carbamic acid dimethyl-ethyl ester as a colorless oil. TLC, 15:85-isopropyl alcohol:methylene chloride, <math>R_f=0.54$. 1H NMR (300 MHz, CDCl3) δ 8.46-8.56 (m, 4H), 7.53-7.62 (m, 2H), 7.22-7.31 (m partially obscured, 2H), 7.05-7.18 (m, 3H), 4.90 (s, 2H), 4.77 (s, 2H), 4.75-4.99 (m partially obscured, 1H), 3.69-3.83 (br m, 1H), 3.05-3.25 (br m, 1H), 2.70-2.96 (m, 2H), 1.45 (s, 18H), 1.44 (s, 9H), 1.20-2.03 (m, 4H); ^{13}C NMR (75 MHz, CDCl3) δ 166.8, 154.0, 152.6, 149.1, 149.0, 148.6, 144.9, 144.7, 138.9, 138.7, 135.1, 133.1, 132.4, 131.9, 128.7, 125.7, 125.6, 125.3, 123.6, 82.5, 82.2, 51.2, 49.4, 42.6, 33.9, 28.4, 28.2, 28.0; MS (CI) m/z 702 (M+H).

B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{5-[(pyridin-3-ylmethyl)-amino]-pyridin-3-yl}-methanone tetrahydrochloride

{5-[1-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-pyridin-3-ylmethyl-carbamic acid dimethyl-ethyl ester (0.0250 g, 0.0356 mmol) was treated with 5-6 M HCl in isopropanol (1.0 mL, 8.0 mmol) and stirred at ambient temperature. After 90 minutes the reaction mixture was diluted with methyl alcohol (0.5 mL) and stirring was continued for an additional 75 minutes. Dripping the reaction solution into ether (40 mL) with vigorous stirring afforded a white precipitate which was collected by filtration, washed with fresh ether (3.0 mL), and dried to afford 1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-{5-[(pyridin-3-ylmethyl)-amino]-pyridin-3-yl}-methanone tetrahydrochloride (0.0160 g): ¹H NMR (300 MHz, DMSO-d6) δ 8.60-8.95 (m, 2H), 8.39 (br s, 2H), 8.29 (d, J=8.0 Hz, 1H), 7.97-8.25 (m, 2H), 7.65-7.85 (m, 2H), 7.47 (d, J=8.0 Hz, 2H), 7.20-7.38 (m, 3H), 4.63 (s, 2H), 4.43-4.61 (m partially obscured, 1H), 4.00 (AB q, J=5.8 Hz,

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2H), 3.05-3.25 (m partially obscured, 1H), 2.72-2.95 (m, 2H), 1.80-1.88 (m, 1H), 1.47-1.77 (m, 3H); MS (CI) m/z 402 (M+H).

EXAMPLE 113

- 5 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{5-[(pyridin-2-ylmethyl)-amino]-pyridin-3-yl}-</u> methanone tetrahydrochloride
 - A. {5-[1-(4-{3-[*N*,*N*-Bis-(*tert*-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-pyridin-2-ylmethyl-carbamic acid dimethyl-ethyl ester
- By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 2-(chloromethyl)pyridine hydrochloride in place of 4-bromo-2-fluorobenzyl bromide, there was prepared {5-[1-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-pyridin-2-ylmethyl-carbamic acid dimethyl-ethyl ester as a colorless oil. TLC, 50:50-methylene chloride:ethyl acetate, R_f= 0.09. ¹H NMR (300 MHz, CDCl₃) δ 8.67 (d, J=2.3 Hz, 1H), 8.52 (d, J=4.7 Hz, 1H), 8.44 (d, J=1.8 Hz, 1H), 7.81 (s, 1H), 7.59-7.72 (m, 1H), 7.22-7.31 (m partially obscured, 2H), 7.00-7.20 (m, 4H), 4.97 (s, 2H), 4.77 (s, 2H), 4.72-4.90 (m partially obscured, 1H), 3.74-3.89 (br m, 1H), 3.04-3.25 (br m, 1H), 2.69-2.94 (m, 2H), 1.45 (s, 18H), 1.41 (s, 9H), 1.23-2.03 (m partially obscured, 4H); MS (CI) m/z 702 (M+H).
- 20 B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{5-[(pyridin-2-ylmethyl)-amino]-pyridin-3-yl}methanone tetrahydrochloride

 By proceeding in a similar manner to the method described in EXAMPLE 112B, but using {5-[1-(4-{3-

[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidin-1-yl)-methanoyl]-pyridin-3-yl}-pyridin-2-ylmethyl-carbamic acid dimethyl-ethyl ester, there was prepared 1-[4-(3-aminomethyl-

phenyl)-piperidin-1-yl]-1-{5-[(pyridin-2-ylmethyl)-amino]-pyridin-3-yl}-methanone tetrahydrochloride as a white solid. MS (ESI) m/z 402 (M+H).

In a similar manner to the methods described in EXAMPLES 105 and 112, the following compounds are prepared:

EXAMPLE 114

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{5-[(pyridin-4-ylmethyl)-amino]-pyridin-3-yl}-methanone tetrahydrochloride;

EXAMPLE 115.

35 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-benzylamino-phenyl)-methanone dihydrochloride;

A. [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105B, but using 3-(Bocamino)benzoic acid in place of 5-tert-butoxycarbonylamino-nicotinic acid, there was prepared [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid tert-butyl ester as a white solid. ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.50 (m, 2H), 7.22-7.37 (m, 2H), 7.04-7.15 (m, 4H), 4.77-4.90 (br m, 1H), 4.76 (s, 2H), 3.81-3.96 (br m, 1H), 3.05-3.20 (br m, 1H), 2.68-2.90 (m, 2H), 1.52 (s, 9H), 1.45 (s, 18H), 1.35-1.85 (m partially obscured, 4H)); MS (CI) m/z 610 (M+H).

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B. Benzyl-[3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using benzyl bromide in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[N,N-bis-(tert-

butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared benzyl-[3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester as a white solid. ¹H NMR (300 MHz, CDCl₃) δ 7.03-7.34 (m, 13H), 4.84 (br s, 2H), 4.78-4.90 (m partially obscured, 1H), 4.77 (s, 2H), 3.69-3.85 (br m, 1H), 2.90-3.10 (br m, 1H), 2.65-2.88 (m, 2H), 1.45 (s, 18H), 1.41 (s, 9H), 1.35-1.95 (m partially obscured, 4H)); MS (CI) m/z 700 (M+H).

C. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-benzylamino-phenyl)-methanone dihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using prepared benzyl-[3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared 1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-(3-benzylamino-phenyl)-methanone dihydrochloride as a white solid. MS (ESI) m/z 400 (M+H).

EXAMPLE 116

30 <u>1-{4-(3-Aminomethyl-phenyl)-piperidin-1-yl}-1-{3-[(naphthalen-2-ylmethyl)-amino]-phenyl}-</u> methanone dihydrochloride;

A. [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-naphthalen-2-ylmethyl-carbamic acid tert-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 2-(bromomethyl)naphthalene in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[N,N-bis-

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(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-naphthalen-2-ylmethyl-carbamic acid *tert*-butyl ester as a white solid. MS (ESI) m/z 650 (M+H).

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B. 1-{4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(naphthalen-2-ylmethyl)-amino]-phenyl}-methanone dihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-naphthalen-2-ylmethyl-carbamic acid tert-butyl ester, there was prepared 1-{4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(naphthalen-2-ylmethyl)-amino]-phenyl}-methanone dihydrochloride as a white solid. MS (ESI) m/z 450 (M+H).

EXAMPLE 117

3-[(3-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-phenylamino)-methyl]-benzonitrile dihydrochloride;

A. [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-(3-cyano-benzyl)-carbamic acid tert-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using α-bromom-tolunitrile in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[N,N-bis-(tertbutoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid tert-butyl ester,
there was prepared [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1carbonyl)-phenyl]-(3-cyano-benzyl)-carbamic acid tert-butyl ester as a white solid. MS (CI) m/z 725
(M+H).

B. 3-[(3-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-phenylamino)-methyl]-benzonitrile dihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-(3-cyano-benzyl)-carbamic acid tert-butyl ester, there was prepared 3-[(3-{1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-phenylamino)-methyl]-benzonitrile dihydrochloride as a white solid. MS (ESI) m/z 425 (M+H).

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EXAMPLE 118

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(4-bromo-benzylamino)-phenyl]-methanone dihydrochloride;

- A. (4-Bromo-benzyl)-[3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid tert-butyl ester
- By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 4-
- bromobenzyl bromide in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared (4-bromo-benzyl)-[3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester as a clear oil. MS (CI) m/z 778 (M+H).
- 10 B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(4-bromo-benzylamino)-phenyl]-methanone dihydrochloride
 - By proceeding in a similar manner to the method described in EXAMPLE 105D, but using (4-bromobenzyl)-[3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid tert-butyl ester, there was prepared 1-[4-(3-aminomethyl-phenyl)-piperidin-1-
- 15 <u>yl]-1-[3-(4-bromo-benzylamino)-phenyl]-methanone dihydrochloride</u> as a white solid. MS (ESI) m/z 480 (M+H).

EXAMPLE 119

- 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(pyridin-2-ylmethyl)-amino]-phenyl}-methanone trihydrochloride;
 - A. [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-pyridin-2-ylmethyl-carbamic acid tert-butyl ester
- By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 2-picolyl chloride hydrochloride in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-pyridin-2-ylmethyl-carbamic acid *tert*-butyl ester as a white solid. ¹H NMR (300 MHz, CDCl₃): δ 8.53 (d, 1H), 7.60-7.70 (m, 2H), 7.29-7.37 (m, 4H), 7.08-7.24 (m, 5H), 4.97 (s, 2H),
- 4.70-4.90 (m partially obscured, 1H), 4.77 (s, 2H), 3.75-3.95 (br m, 1H), 2.65-3.20 (br m, 3H), 1.40-2.00 (m partially obscured, 4H), 1.45 (s, 18H), 1.39 (s, 9H). MS (ESI): m/z 701 (M+H).
 - B. 1-{4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(pyridin-2-ylmethyl)-amino]-phenyl}-methanone trihydrochloride
- By proceeding in a similar manner to the method described in EXAMPLE 105D, but using [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-pyridin-2-

yl]-1-{3-[(pyridin-2-ylmethyl)-amino]-phenyl}-methanone trihydrochloride as a light yellow solid. ¹H NMR [300 MHz, (CD₃)₂SO]: δ 8.69 (d, 1H), 8.34 (br s, 3H), 8.19 (tr, 1H), 7.73 (d, 1H), 7.63 (tr, 1H), 7.25-7.42 (m, 4H), 7.14 (tr, 1H), 6.68 (d, 1H), 6.61 (m, 2H), 4.40-4.70 (br m partially obscured, 1H), 4.61 (s, 2H), 4.01 (q, 2H), 3.70-3.95 (br m partially obscured, 1H), 2.90-3.15 (br m, 1H), 2.65-2.90 (br m, 2H), 1.35-1.95 (br m, 4H). MS (ESI): m/z 401 (M+H).

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EXAMPLE 120

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(pyridin-3-ylmethyl)-amino]-phenyl}-methanone trihydrochloride;

A. [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-pyridin-3-ylmethyl-carbamic acid tert-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 3-picolyl chloride hydrochloride in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[*N*,*N*-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared [3-(4-{3-[*N*,*N*-bis-(*tert*-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-pyridin-3-ylmethyl-carbamic acid *tert*-butyl ester as a cream oil. ¹H NMR (300 MHz, CDCl₃): δ 8.49 (br s, 2H), 7.57 (d, 1H), 7.33 (m, 1H), 7.07-7.24 (m, 8H), 4.70-4.95 (m partially obscured, 1H), 4.85 (s, 2H), 4.77 (s, 2H), 3.65-3.90 (br m, 1H), 2.65-3.15 (br m, 3H), 1.40-2.00 (m partially obscured, 4H), 1.45 (s, 18H), 1.41 (s, 9H). MS (ESI): m/z 701 (M+H).

B. 1-{4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(pyridin-3-ylmethyl)-amino]-phenyl}-methanone trihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using [3-(4-{3-[*N,N*-Bis-(*tert*-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-pyridin-3-ylmethyl-carbamic acid *tert*-butyl ester, there was prepared 1-{4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(pyridin-3-ylmethyl)-amino]-phenyl}-methanone trihydrochloride as a light yellow solid. ¹H NMR [300 MHz, (CD₃)₂SO]: δ 8.81 (s, 1H), 8.70 (d, 1H), 8.34 (m, 4H), 7.86 (tr, 1H), 7.25-7.41 (m, 4H), 7.14 (tr, 1H), 6.67 (d, 1H), 6.59 (m, 2H), 4.40-4.70 (br m partially obscured, 1H), 4.50 (s, 2H), 4.01 (q, 2H), 3.70-3.90 (br m partially obscured, 1H), 2.90-3.15 (br m, 1H), 2.65-2.90 (br m, 2H), 1.35-1.95 (br m, 4H). MS (ESI): m/z 401 (M+H).

EXAMPLE 121

35 <u>1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(pyridin-4-ylmethyl)-amino]-phenyl}-methanone</u> trihydrochloride.

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A. [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-pyridin-4-ylmethyl-carbamic acid tert-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 4-picolyl chloride hydrochloride in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)-phenyl]-phenyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-pyridin-4-ylmethyl-carbamic acid *tert*-butyl ester as a cream oil. ¹H NMR (300 MHz, CDCl₃): δ 8.55 (br d, 2H), 7.33 (q, 2H), 7.06-7.26 (m, 8H), 4.70-4.90 (m partially obscured, 1H), 4.84 (s, 2H), 4.77 (s, 2H), 3.70-3.90 (br, 1H), 268-3.15 (br m, 3H), 1.40-2.00 (m partially obscured, 4H), 1.45 (s, 18H), 1.41 (s, 9H). MS (ESI): m/z 701 (M+H).

B. 1-{4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(pyridin-4-ylmethyl)-amino]-phenyl}-methanone trihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-pyridin-4-ylmethyl-carbamic acid tert-butyl ester, there was prepared 1-{4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(pyridin-4-ylmethyl)-amino]-phenyl}-methanone trihydrochloride as a cream solid. ¹H NMR [300 MHz, (CD₃)₂SO]: δ 8.76 (br s, 2H), 8.33 (br s, 3H), 7.87 (d, 2H), 7.24-7.41 (m, 4H), 7.13 (tr, 1H), 6.65-7.00 (br, 1H), 6.56-6.64 (m, 3H), 4.40-4.70 (br m partially obscured, 1H), 4.61 (s, 2H), 4.01 (q, 2H), 3.70-3.90 (br m partially obscured, 1H), 2.90-3.15 (br m, 1H), 2.65-2.90 (br m, 2H), 1.35-1.95 (br m, 4H). MS (ESI): m/z 401 (M+H).

EXAMPLE 122

25 3-[1-(5-Phenylethynyl-furan-2-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate

A. 4-oxo-piperidine-1-carboxylic acid (trimethylsilyl) ethyl ester

A solution of 4-piperidone monohydrate. Hydrochloride (13.55g, 88mmol) 2-trimethylsilylethyl-p-nitrophenylcarbonate (25.00g, 88mmol) in acetonitrile (300 ml) was treated with triethylamine (50 ml, 359 mmol) and dimethyl-aminopyridine (10.78g, 88mmol) and heated to reflux for 2 hours. The solution was cooled and concentrated to an oil. The residue was dissolved in dichloromethane (300ml) and washed twice with 1M hydrochloric acid and twice with 1M sodium hydroxide until all of the yellow color was removed from the organics. The organics were then washed with brine, dried over magnesium sulfate and concentrated under vacuum to give 4-oxo-piperidine-1-carboxylic acid (trimethylsilyl) ethyl ester as colorless oil. (19.35g) ¹H NMR (CDCl₃, 300 MHz): δ 4.24 (2H, t), 3.78 (4H, t), 2.45 (4H, t), 1.05 (2H, t), 0.05 (9H, s) MS (EI) 284(M+CH₃CN)

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B. 4-(3-Cyano-phenyl)-3,6-dihydro-2H-pyridine-1-carboxylic acid 2-trimethylsilanyl-ethyl ester A solution of lithium hexamethyldisilazide (60 mmol) in anhydrous tetrahydrofuran (150 ml), at -78°C, was treated dropwise with a solution of 4-oxo-piperidine-1-carboxylic acid (trimethylsilyl) ethyl ester (13.30g, 55mmol) in anhydrous tetrahydrofuran (50ml). The addition was over 20 minutes maintaining the internal temperature at -65 to -70°C. This solution was stirred at -78°C for 45 minutes and then treated with a solution of N-phenyltrifluoromethanesulfonimide (19.65g, 55mmol) in anhydrous tetrahydrofuran (75ml). The solution was warmed to 0°C, then stirred at 0°C for 3 hours and then concentrated under vacuum. The residue was dissolved in dichloromethane and washed with water, dried over magnesium sulfate and concentrated to give 2-(trimethylsilyl) ethyl 1,2,3,6tetrahydro-4- (trifluoromethylsulphonyloxy)-pyridine-1-carboxylate as a yellow oil (22.1g). The material is used crude, as column chromatography on silica gel or alumina caused the material to deteriorate. A portion of this material (20.65g, 55mmol) was dissolved in acetonitrile (300 ml) and the solution was treated with 3-cyanoboronic acid (8.90g, 60mmol), 2M sodium carbonate (82.5ml, 165mmol) and lithium chloride (6.98g, 165mmol). The non-homogenous mixture was stirred vigorously and flushed with nitrogen for 5 minutes, then tetrakistriphenylphospine palladium (0) (3.10g, 3mmol). The mixture was heated to reflux (90°C oil bath) for 90 minutes, then cooled and filtered. The red filtrate was concentrated and the residue was partitioned between dichloromethane (3. lots 100ml) and 2M sodium carbonate (200ml). The combined organic extracts were dried over magnesium sulfate and then concentrated under vacuum. The resultant oil was subjected to chromatography silica gel eluting with a mixture of ethyl acetate, heptane and dichloromethane (1:5:1, v/v) to yield 4-(3-cyano-phenyl)-3,6-dihydro-2H-pyridine-1-carboxylic acid 2-trimethylsilanyl-ethyl ester as a yellow oil (10.46g). ¹H NMR (CDCl₃, 300 MHz): 8 7.40-7.65 (m, 4H), 6.10 (m, 1H), 4.23 (t, 2H), 4.15 (d, 2H), 3.70 (t, 2H), 2.45 (m, 2H), 1.12 (t, 2H), 0.05 (s, 9H).

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C. 4-(3-Aminomethyl-phenyl)-piperidine-1-carboxylic acid 2-trimethylsilanyl-ethyl ester hydrochloride

4-(3-Cyanophenyl)-3,6-dihydro-2H-pyridine-1-carboxylic acid 2-trimethylsilanyl-ethyl ester (10.40g, 32mmol) was dissolved in ethanol (250ml), concentrated hydrochloric acid (3ml, 35mmol) and 10% palladium on carbon (50% wet, 5.0g) was added. The mixture was hydrogenated at 50 psi for 4 hours then filtered through celite and concentrated. The oily solid obtained was triturated with ether/pentane and 4-(3-aminomethyl-phenyl)-piperidine-1-carboxylic acid 2-trimethylsilanyl-ethyl ester hydrochloride was obtained as a white solid (7.10g). ¹H NMR [(CD₃)₂SO, 300 MHz]: δ 8.38 (br s, 2H), 7.20-7.40 (m, 4H), 4.10 (t, 4H), 3.98 (s, 2H), 2.63-3.00 (m, 3H), 1.75 (m, 2H), 1.50 (m, 2H), 0.94 (t, 2H), 0.02 (s, 9H). LC-MS (ES) 335 (M⁺+H), 93% TIC.

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D. (3-Piperidin-4-yl-benzyl) carbamate Wang resin

p-Nitrophenyl carbonate Wang resin (11.00g, 15mmol) and anhydrous dimethylformamide (100ml) were placed in a peptide synthesis vessel and the resin was allowed to swell for 15 minutes. This was then treated with 4-(3-aminomethyl-phenyl)-piperidine-1-carboxylic acid 2-trimethylsilanyl-ethyl ester hydrochloride (7.50g, 21mmol) in 50ml dimethylformamide, dimethylaminopyridine (0.72, 6mmol) and diisopropylethyl-amine. The peptide vessel was shaken at room temperature for 24 hours, then washed thoroughly with dimethylformamide (x5), methanol (x2), dimethylformamide (x2), methanol (x2), methanol (x2), dichloromethane (x3), and dried. The resin was then treated with tetrahydrofuran to swell the resin and then allowed to drain. Then anhydrous tetrahydrofuran (100ml) and tetrabutylammonium fluoride (75ml, 1M in tetrahydrofuran) were added and the resin shaken for 18 hours. The resin was drained and washed with tetrahydrofuran (x5), methanol (x3), dichloromethane (x3), methanol (x3), dichloromethane (x3) and dried to give (3-piperidin-4-yl-benzyl) carbamate Wang resin (12.30g).

E. 3-[1-(5-Phenylethynyl-furan-2-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate
(3-Piperidin-4-yl-benzyl) carbamate Wang resin (60mg, 0.075mmol) suspended in dimethylformamide
(3ml) and 5-phenylethynyl-furan 2 carboxylic acid (80mg, 0.38mmol), diisopropylcarbodiimide
(48mg, 0.38mmol) and 1-hydroxybenzotriazole (50mg, 0.38mmol) were added. The mixture was
shaken at room temperature overnight and washed with dimethylformamide (x5), methanol (x5),
dichloromethane then methanol (repeat 5 times). The resin was treated with trifluoroacetic acid and
dichloromethane (1:1 v/v, 4ml) for 45 minutes and filtered. The filtrate was concentrated to give 3-[1(5-phenylethynyl-furan-2-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate as a pale yellow oil
(30mg). LC-MS (ES) 385 (M[†]+H) 100% TIC.

In a similar manner to the methods described in EXAMPLE 112, the following compounds set forth in Table 5 were prepared as the trifluoroacetate salts:

TABLE 5

EG	Structure	M/Z	MS area %	EG	Structure	M/Z	MS area %
123	NH ₂	365.2	93	124	NH ₂	381.4	100

125	NH ₂	430.2	100	126	NH,	413.1	100
""		150.2	100	120		413.1	
	OH OH				Q a		
			<u>'</u>				Ì
	N K) - a		
127	NH	418.2	100	128	O NH	299.3	100
	\downarrow						
	N Br NO ₂				X		
129	NHY	408.3	94	130	NH ₃	349.1	100
	Ĭ				 		
	N NO.						
	° C						
131	NH,	311.1	90	132	F NH ₂	313.1	100
	X						
		ļ			(N) 0, N, -0-		
	•						
133	OH OH	385.2	100	134	NH ₃	395.1	100
	\bigcirc				\bigcirc		
	CH,				•		
	He-0						
135	NH ₂	285.1	100	136	NAPS CI	363	100
		203.1	100	100			100
	$\overline{}$	į					
125	NH	220.1	100	120	Br NH.	2011	100
137	5	330.1	100	138		301.1	100
				1			
			}				
	NO						
139	NH ₂	315.1	100	140	NH ₂	315.1	100
	Y						
	CHY, M]	
			-		1 0 m		
1	NH.	100: :	100	142	NH.	005:	70
141		301.1	100	142		285.1	79
					ΙX		
							ĺ
	C. C.				170		
نــــــــــــــــــــــــــــــــــــــ			J	<u> </u>	L	L	L

143	NH ₂	335.1	100	144	kh².	348.2	100
143		333.1	100	144		340.2	100
145	Note of the control o	379.2	100	146	NH ₃	303.1	100
147	NO ₃ NH ₂ CH ₃ N H ₃ C N N N N N N N N N N N N N	365.2	100	148	NH ₂	422.2	100
149		379.2	99	150		337.2	99
151	NH ₃	353.3	100	152		418.2	99
153		353.2	99	154	NH ₂	336.3	89
155		378.2	61	156	NH,	345.2	100
157	NH ₃	440.3	100	158	Br.————————————————————————————————————	459	100

159	NH ₃	305.2	100	160	NH ₂	379.2	80
					\bigcirc		
	N CH,						
161	NH,	364.2	100	162	NH ₂	476.2	100
					Y		
					Q		
	N-M-CH, N				of shift		
163	H ₂ C-V	346.2	100	164	NH ₂	330.2	100
103		340.2	100	104		330.2	100
<u>'</u>					Ĭ		
<u> </u>							
	T) on						
165	NH ₂	368.2	100	166	ČI ŅH,	331.2	100
103		308.2	100	100		331.2	100
	l Ă	ļ					
167	NH ₂	364.2	100	168	P NH ₂	387.2	100
					\bigcirc		
	Ci V				a v	ļ	
169	cr N	391	94	170	N—	366.1	95
109		391	24	170	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	300.1	93
	Br Br						
171	P F	498.9	100	172	N—\	351.2	66
			200				
	l I						
	_						
	Br						
152	T T	201.0	100	1=1	N	2050	100
173		321.2	100	174		335.2	100
		1		1	<u>_</u>		
175	<u>N</u>	349.1	100	176	N\	354.2	100
				1			
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	0=				o. N=o		
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	 	100				
177	313.1	100	178		321.2	84
179	429.1	81	180	N C C C C C C C C C C C C C C C C C C C	378.1	100
181	351.2	100	182		381.2	85
183	313.2	100	184	0 CI O CI	374.1	100
185	331.2	100	186		342	84
187	420.1	100 -	188	O=N°	358.1	100
189	309.1	100	190		355.2	100
191	284.2	100	192		324.2	81
193	336.2	19	194	N—————————————————————————————————————	313.1	95

195		220.1	89	196		299.2	100
					0=		
197		369.2	100	198		315.2	100
199	NNo-	355.1	92	200		331.2	100
201		327.2	100	202		463.1	100
203	a	440.1	94	204		355.2	100
205		351.2	100	206		363.1	100
207		337.2	100	208		339.2	54

209	/=\	361.2	65	220	N—	340.2	97
211		313.2	100	212		369.2	100
213		413.1	100	214		381.2	62
215		359.2	94	216		371.1	100
217		429.1	100	218	N—————————————————————————————————————	433.1	100
219		315.2	100	220		400.2	100
221	Comment	337.2	100	222		375.1	100

223	N	445	100	224	SY'	289.1	100
	F Br						
225		339.2	100	226	N N	259.2	100
227		315.2	100	228		349.2	86
229		339.3	100	230		353.3	100
231		329.3	100	232		381.2	93
233	o FF	389.2	94	234		335.2	100
235		362.2	71	236		367.2	100

237		317.2	100	238		407.3	100
		017.2	100	250		407.3	100
222	N	004.0		2.40	N		
239		331.2	100	240		343.3	100
241		313.2	100	242		391.3	100
243	0=-N	399.2	100	244		407.2	100
245		321.2	100	246	Chiral O NO	422.3	88
247		327.2	100	248		397.3	91

249	Ŋ	425.2	80	250	N-\	363.1	100
251		337.2	90	252		408.2	60
253		327.2	96	254		323.2	100
255	»	385.2	100	256		389.2	100
257		261.2	100	258	0=N-0	354.2	100
259	N—————————————————————————————————————	415.2	100	260	FF FF	431.2	100
261	F-F-F-F-F-F-F-F-F-F-F-F-F-F-F-F-F-F-F-	381.2	91	262		417.2	100
263		387.2	100	264	0 2 2	290.2	100

265		357.2	100	266	N	355.2	91
267	a ci	344.2	83	268		442.2	100
269		339.2	100	270		377.3	78
271	Br.	428.2	44	272		367.3	100
273		383.3	100	274	0=N° 0-	370.2	100
275		383.3		276	N CI	343.2	95
277		325.2	100	278	O N	373.1	100

By proceeding in a similar manner to the method described in EXAMPLE 36, but using the
appropriate carboxylic acid derived TFP resin in place of the 3,4-dichlorobenzoic acid TFP resin, the
following compounds set forth in Table 6 were prepared as the trifluoroacetate salts:

TABLE 6

EG	Structure	M/Z	MS area	EG	Structure	M/Z	MS area
282	NH ₂	273.3	>95%	283	NH ₃	369.2	>95%
284	NH ₃	377.4	>95%	285	NH, CN,	379.3	>95%
286	NH, CON	349.3	>95%	287	NH ₂ N N CI	422.3, 424.3	>95%
288	NH, CN, CV	351.3	>95%	289	NH ₂ NH ₂	302.2	>95%
290	NH. CONT.	399.3	>95%	291	NH ₂	429.3	>95%
292	NH ₂ N	399.3	>95%	293	NH ₂	355.2	>95%
294	NH ₂ CN	320.3	>95%	295	NH, CH, CP	383.3	>95%
296	NH ₂	387.3	>95%	297	NH ₃	367.3	85%

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298	NH ₂	386.3	>95%	299	NH ₂	385.2	>95%
300	NH, CN HO	335.3	>95%	301	NH ₁	275.2	>95%
302	NH ₂	289.3	>95%	303	NH ₂	289.3	>95%
304	NH, NH,	399.3	90%	305	NH, N	457.3	60%
306	NH, NH,	337.3	>95%	307	NH ₂ NH ₃	262.2	>95%
308	\$	381.3	>95%	309	NH ₂ N _O O _O O _O	339.2	75%
310	NH, CN	298.3	>95%	311	NH ₁	322.3	>95%
312	NH ₂ N ₁ N ₂ N ₂ N ₃ N ₃ O ₃	359.3, 360.3	75%	313	NH, CN, CV	357.4	>95%
314	NH ₃	393.3	>95%	315	NH ₂	347.3	>95%
316	NH, CNXOCI	387.3, 389.3	>95%	317	NH, CN, CM	346.3	>95%
318	NH ₂	275.3	>95%	319	NH ₂ CN ₂ CN	360.3	90%
320	NH ₂ N ₁ O ₀	351.3	>95%	321	NH2 CN JN N-C	376.2	>95%
322	NH ₂ CN	381.3	90%	323	NH, CA	365.2	65%
324	NH ₂ NMe,	364.3	>95%	325	NH ₂	443.2, 445.2	75%
326	NH ₂	271.2	>95%	327	NH ₂	233.2	>95%
328	NH ₂	365.3	>95%	329	NH ₂	357.3	>95%
330	NH, CN	399.3	70%	331	NH ₂	375.3	>95%

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332	NH2 N T S	379.3	80%	333	NH, CN LIN	398.2, 400.2	>95%
334	NH, NY CO	365.3	>95%	335	MH ₃ N C N	403.3	>95%
336	NOTO,	385.2, 387.2	>95%	337	NH ₂ N _N	437.3, 439.3	>95%
338	NH, CN, CO	401.3	>95%	339	NH ₂	352.3	>95%
340	NH, CN,	351.3	>95%	341	NH ₂	349.3	>95%
342	NH ₂ N S	341.2	>95%	343	NH ₂ N ₃ SS	357.2	>95%

EXAMPLE 344

[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-[1,1';4',1"]terphenyl-3-yl-methanone hydrochloride

5 A. {4-[3-N,N-Di-(tert-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-(3-bromo-phenyl)-methanone

By proceeding in a similar manner to the method described in EXAMPLE 105B, but using 3-bromobenzoic acid in place of 5-tert-butoxycarbonylamino-nicotinic acid, there was prepared {4-[3-N,N-di-(tert-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-(3-bromo-phenyl)-methanone as a colorless oil. MS (CI) m/z 573 (M+H).

B. {4-[3-*N*,*N*-Di-(*tert*-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-[1,1';4',1"]terphenyl-3-yl-methanone

By proceeding in a similar manner to the method described in EXAMPLE 17D, but using 4-biphenylboronic acid in place of 1-(5-phenylethyl-pyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6-tetrahydro-pyridine and {4-[3-N,N-di-(tert-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-(3-bromo-phenyl)-methanone in place of N-(tert-butoxycarbonyl)-3-bromo-4-fluoro-benzylamine, there was prepared {4-[3-N,N-di-(tert-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-[1,1';4',1"]terphenyl-3-yl-methanone as a yellow oil. MS (CI) m/z 647 (M+H).

C. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-[1,1';4',1"]terphenyl-3-yl-methanone hydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using {4-[3-N,N-di-(tert-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-[1,1';4',1"]terphenyl-3-yl-methanone,

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there was prepared [4-(3-aminomethyl-phenyl)-piperidin-1-yl]-[1,1';4',1"]terphenyl-3-yl-methanone hydrochloride as a cream-colored solid. MS (CI) m/z 447 (M+H).

EXAMPLE 345

5 3-[1-(6-Chloroquinoline-3-carbonyl)-piperidin-4-yl]-benzylamine di-hydrochloride

A. Ethyl 6-chloroquinoline-3-carboxylate

Ethyl 4,6-Dichloroquinoline-3-carboxylate [prepared as described in C. C. Price and R. M. Roberts J. Amer. Chem. Soc. 68, 1204 (1964); C. J. Ohnmacht, Jr. J. Med. Chem. 14, 17 (1971)] (2.0 g, 7.4 mmol) was added portionwise to a solution of sodium borohydride (1.2 g, 31mmol) in 15 ml of methoxyethanol at about 0°C. The reaction mixture was warmed to room temperature over 3 hours then diluted with ethyl acetate. After standard aqueous workup (dil HCl; saturated NaHCO₃) the organic layer was dried (NaSO₄) and concentrated to a residue. The residue was exposed to air oxidation (about 14 days) and extracted repeatedly with boiling heptane. The heptane was removed in vacuo to yield ethyl 6-chloroquinoline-3-carboxylate as a beige solid. ¹H NMR [(CDCl₃), 300 MHz]: δ 9.38 (bs, 1H), 8.68 (s, 1H), 8.05 (d, 1H), 7.83 (s, 2H), 7.69 (d, 1H), 4.40 (q, 2H), 1.39 (t, 3 H). MS(EI): 236(M⁺+ H).

B. 6-Chloroquinoline-3-carboxylic acid

Ethyl 6-chloroquinoline-3-carboxylate (0.19 g, 0.81 mmol) was saponified by treatment with dioxane (10 ml) and 10% aqueous sodium hydroxide (10 ml) at reflux for 3 hours. The dioxane was removed under vacuo; the aqueous solution remaining was acidified with HCl. The precipitated product was collected and washed with water to isolate 6-chloroquinoline-3-carboxylic acid as an off-white solid (0.14 g, 0.67 mmol). ¹H NMR [(CD₃OD), 300 MHz]: δ 9.35 (s, 1H), 8.95 (s, 1H), 8.17 (s, 1H), 8.1 (d, 2H), 7.87 (d, 1H).

C. N,N-bis-(tert-butoxycarbonyl)-3-[1-(6-chloroquinoline-3-carbonyl)-piperidin-4-yl] benzylamine By proceeding in a similar manner to the method described in EXAMPLE 1C, but using 6-chloroquinoline-3-carboxylic acid in place of 5-phenylethynyl-pyridine-3-carboxylic acid, crude title compound was prepared. The crude product was purified by flash chromatography (25-50% ethyl acetate/Heptane) to yield the title compound as a white amorphous solid. ¹H NMR[(CDCl₃), 300 MHz]: δ 8.98 (bs, 1H), 8.20 (s, 1H), 8.05 (d, 1H), 7.88 (s, 1H), 7.72 (d, 1H), 7.08-7.31 (m, 4H), 4.93 (br m, 1H), 4.78 (s, 2H), 3.90 (br m, 1H), 3.27 (br m, 1H), 3.95 (br m, 1H), 2.82 (m, 1H), 1.6-2.1 (br m, 4H), 1.47 (s, 18H).

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D. 3-[1-(6-Chloroquinoline-3-carbonyl)-piperidin-4-yl]-benzylamine

N,N-bis-(tert-butoxycarbonyl)-3-[1-(6-Chloroquinoline-3-carbonyl)-piperidin-4-yl] benzylamine (0.055 g, 0.095 mmol) was treated with a solution of 15% trifluoroacetic acid in methylene chloride (5 ml) at 0°C. The reaction was warmed to ambient temperature over 2.5 hr and the solvents were removed in vacuo. The residue was triturated with ether to yield the title compound (0.033 g, 0.087mmol) as an amorphous solid. ¹H NMR[(CD₃)₂SO, 500 MHz]: δ 8.95 (s, 1H), 8.44 (s, 1H), 8.20 (s, 1H), 8.07 (d, 1H), 7.84 (d, 2H), 7.23-7.40 (m, 4H), 4.67 (m, 1H), 7.34 (m, 3H), 4.75 (br m, 1H), 4.05 (m, 2H), 3.75 (br m, 1H), 3.30 (br m, 1H), 2.80-3.00 (br m, 2H), 1.90 (br m, 1H), 1.6-1.8 (br m, 3H). MS(EI): 380(M⁺+H).

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EXAMPLE 346

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-benzylamino-phenyl)-methanone dihydrochloride

A. [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105B, but using 3-(Bocamino)benzoic acid in place of 5-tert-butoxycarbonylamino-nicotinic acid, there was prepared [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid tert-butyl ester as a white solid. ¹H NMR (300 MHz, CDCl₃): δ 7.40-7.50 (m, 2H), 7.22-7.37 (m, 2H), 7.04-7.15 (m, 4H), 4.75-4.90 (br m, 1H), 4.76 (s, 2H), 3.80-3.96 (br m, 1H), 3.00-3.25 (br m, 1H), 2.68-2.95 (m, 2H), 1.40-2.05 (m partially obscured, 4H), 1.52 (s, 9H), 1.45 (s, 18H). MS (CI): m/z 610 (M+H).

B. Benzyl-[3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using benzyl bromide in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared benzyl-[3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-

30 <u>1-carbonyl)-phenyl]-carbamic acid tert-butyl ester</u> as a white solid. ¹H NMR (300 MHz, CDCl₃): δ 7.03-7.34 (m, 13H), 4.75-4.90 (m partially obscured, 1H), 4.84 (br s, 2H), 4.77 (s, 2H), 3.69-3.85 (br m, 1H), 2.90-3.10 (br m, 1H), 2.65-2.90 (m, 2H), 1.40-2.00 (m partially obscured, 4H), 1.45 (s, 18H), 1.41 (s, 9H). MS (CI): m/z 700 (M+H).

35 <u>C. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-benzylamino-phenyl)-methanone</u> dihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using prepared benzyl-[3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared 1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-(3-benzylamino-phenyl)-methanone dihydrochloride as a white solid. ¹H NMR [300 MHz, (CD₃)₂SO]: δ 8.26 (br s, 3H), 7.20-7.55 (m, 9H), 7.11 (tr, 1H), 6.66 (d, 1H), 6.57 (m, 2H), 4.40-4.70 (br m, 1H), 4.30 (s, 2H), 4.15 (m, 1H), 4.01 (q, 2H), 2.90-3.15 (br m, 1H), 2.65-2.90 (br m, 2H), 1.35-1.95 (br m, 4H). MS (ESI): m/z 400 (M+H).

EXAMPLE 347

10 <u>1-{4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(naphthalen-2-ylmethyl)-amino]-phenyl}-</u> methasone dihydrochloride

A. [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-naphthalen-2-ylmethyl-carbamic acid tert-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 2(bromomethyl)naphthalene in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)-phenyl]-carbamic acid tert-butyl ester, there was prepared [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1carbonyl)-phenyl]-naphthalen-2-ylmethyl-carbamic acid tert-butyl ester as a white solid. ¹H NMR
(300 MHz, CDCl₃): δ 7.61-7.80 (m, 4H), 7.38-7.45 (m, 3H), 6.99-7.34 (m, 8H), 5.00 (br s, 2H), 4.704.90 (m partially obscured, 1H), 4.76 (s, 2H), 3.55-3.75 (br m, 1H), 2.70-2.95 (br m, 2H), 2.55-2.70 (m, 1H), 1.40-1.95 (m partially obscured, 4H), 1.45 (s, 18H), 1.42 (s, 9H). MS (ESI): m/z 650 (M+H).

B. 1-{4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(naphthalen-2-ylmethyl)-amino]-phenyl}-methanone dihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-naphthalen-2-ylmethyl-carbamic acid tert-butyl ester, there was prepared 1-{4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[(naphthalen-2-ylmethyl)-amino]-phenyl}-methanone dihydrochloride as a white solid. ¹H NMR [300 MHz, (CD₃)₂SO]: δ 8.22 (br s, 3H), 7.81-7.88 (m, 4H), 7.11-7.54 (m, 8H), 6.69 (d, 1H), 6.59 (s, 1H), 6.54 (d, 1H), 4.45-4.65 (m partially obscured, 1H), 4.47 (s, 2H), 4.01 (q, 2H), 3.60-3.80 (m partially obscured, 1H), 2.85-3.05 (br m, 1H), 2.65-2.85 (br m, 2H), 1.30-1.95 (br m, 4H). MS (ESI): m/z 450 (M+H).

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EXAMPLE 348

3-[(3-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-phenylamino)-methyl]-benzonitrile dihydrochloride

5 A. [3-(4-{3-[N,N-Bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-(3-cyano-benzyl)-carbamic acid tert-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using α-bromo-*m*-tolunitrile in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[*N*,*N*-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared [3-(4-{3-[*N*,*N*-bis-(*tert*-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-(3-cyano-benzyl)-carbamic acid *tert*-butyl ester as a white solid. ¹H NMR (300 MHz, CDCl₃): δ 7.06-7.55 (m, 12H), 4.70-4.90 (m partially obscured, 1H), 4.86 (s, 2H), 4.77 (s, 2H), 3.70-3.90 (br m, 1H), 2.95-3.20 (br m, 1H), 2.65-2.95 (br m, 2H), 1.40-2.00 (m partially obscured, 4H), 1.45 (s, 18H), 1.41 (s, 9H). MS (CI): m/z 725 (M+H).

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B. 3-[(3-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-phenylamino)-methyl]-benzonitrile dihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-(3-cyano-benzyl)-carbamic acid tert-butyl ester, there was prepared 3-[(3-{1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-phenylamino)-methyl]-benzonitrile dihydrochloride as a white solid. ^{1}H NMR [300 MHz, (CD₃)₂SO]: δ 8.18 (br s, 3H), 7.75 (s, 1H), 7.65 (m, 2H), 7.49 (tr, 1H), 7.21-7.35 (m, 4H), 7.08 (tr, 1H), 6.61 (d, 1H), 6.52 (m, 2H), 4.40-4.70 (br m, 1H), 4.33 (s, 2H), 3.98 (q, 2H), 3.50-3.70 (m partially obscured, 1H), 2.85-3.10 (br m, 1H), 2.65-2.85 (br m, 2H), 1.30-1.90 (br m, 4H). MS (ESI): m/z 425 (M+H).

EXAMPLE 349

1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(4-bromo-benzylamino)-phenyl]-methanone dihydrochloride

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A. (4-Bromo-benzyl)-[3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid tert-butyl ester

By proceeding in a similar manner to the method described in EXAMPLE 105C, but using 4-bromobenzyl bromide in place of 4-bromo-2-fluorobenzyl bromide and using [3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester, there was prepared (4-bromo-benzyl)-[3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-

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piperidine-1-carbonyl)-phenyl]-carbamic acid *tert*-butyl ester as a clear oil. ¹H NMR (300 MHz, CDCl₃): δ 7.41 (d, 2H), 7.06-7.38 (m, 8H), 7.10 (d, 2H), 4.70-4.90 (br m, partially obscured, 1H), 4.78 (s, 2H), 4.77 (s, 2H), 4.25-4.45 (br m, 1H), 3.70-3.85 (br m, 1H), 2.90-3.15 (br m, 1H), 2.65-2.90 (br m, 2H), 1.40-2.00 (m partially obscured, 4H), 1.45 (s, 18H), 1.41 (s, 9H). MS (CI): m/z 778 (M+H).

B. 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(4-bromo-benzylamino)-phenyl]-methanone dihydrochloride

By proceeding in a similar manner to the method described in EXAMPLE 105D, but using (4-bromobenzyl)-[3-(4-{3-[N,N-bis-(tert-butoxycarbonyl)amino-methyl]-phenyl}-piperidine-1-carbonyl)-phenyl]-carbamic acid tert-butyl ester, there was prepared 1-[4-(3-aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(4-bromo-benzylamino)-phenyl]-methanone dihydrochloride as a white solid. 1 H NMR [300 MHz, (CD₃)₂SO]: δ 8.28 (br s, 3H), 7.25-7.66 (m, 8H), 7.11 (tr, 1H), 6.64 (d, 1H), 6.55 (m, 2H), 4.45-4.70 (br m, 1H), 4.28 (s, 2H), 4.15 (m, 1H), 4.01 (q, 2H), 2.90-3.15 (br m, 1H), 2.65-2.90 (br m, 2H), 1.30-1.95 (br m, 4H). MS (ESI): m/z 480 (M+H).

EXAMPLE 350

[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-[1,1';4',1"]terphenyl-3-yl-methanone hydrochloride

A. {4-[3-N,N-Di-(tert-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-(3-bromo-phenyl)-methanone

By proceeding in a similar manner to the method described in EXAMPLE 105B, but using 3-bromobenzoic acid in place of 5-*tert*-butoxycarbonylamino-nicotinic acid, there was prepared {4-[3-*N,N*-di-(*tert*-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-(3-bromo-phenyl)-methanone as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.55 (m, 2H), 7.24-7.37 (m, 2H), 7.08-7.16 (m, 4H), 4.75-4.92 (br m, 1H), 4.77 (s, 2H), 3.75-3.90 (br m, 1H), 3.00-3.25 (br m, 1H), 2.70-3.00 (br m, 2H), 1.50-2.00 (m partially obscured, 4H) 1.45 (s, 18H). MS (CI): m/z 573 (M+H).

B. {4-[3-N,N-Di-(tert-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-[1,1';4',1"]terphenyl-3-yl-methanone

By proceeding in a similar manner to the method described in EXAMPLE 17D, but using 4-biphenylboronic acid in place of 1-(5-phenylethyl-pyridine-3-carbonyl)-4-(pinacolatoboronyl)-1,2,3,6-tetrahydro-pyridine and {4-[3-N,N-di-(tert-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-(3-bromo-phenyl)-methanone in place of N-(tert-butoxycarbonyl)-3-bromo-4-fluoro-benzylamine, there was prepared {4-[3-N,N-di-(tert-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-[1,1';4',1"]terphenyl-3-yl-methanone as a yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 7.61-7.71 (m,

8H), 7.34-7.53 (m, 6H), 7.14 (m, 3H), 4.80-5.00 (m, 1H), 4.77 (s, 2H), 3.85-4.05 (br m, 1H), 3.00-3.25 (br m, 1H), 2.70-3.00 (br m, 2H), 1.50-2.05 (m, 4H), 1.44 (s, 18H). MS (CI): m/z 647 (M+H).

C. [4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-[1,1';4',1"]terphenyl-3-yl-methanone hydrochloride By proceeding in a similar manner to the method described in EXAMPLE 105D, but using {4-[3-N,N-di-(tert-butoxycarbonyl)aminomethyl)-phenyl]-piperidin-1-yl}-[1,1';4',1"]terphenyl-3-yl-methanone, there was prepared [4-(3-aminomethyl-phenyl)-piperidin-1-yl]-[1,1';4',1"]terphenyl-3-yl-methanone hydrochloride as a cream-colored solid. ¹H NMR [300 MHz, (CD₃)₂SO]: 8 8.24 (br s, 3H), 7.73-7.84 (m, 8H), 7.29-7.61 (m, 9H), 4.55-4.80 (br m, 1H), 4.01 (q, 2H), 3.65-3.85 (br m, 1H), 2.75-3.05 (br m, 2H), 1.50-2.00 (br m, 4H). MS (CI): m/z 447 (M+H).

EXAMPLE 351

4-(3-Aminomethyl-phenyl)-piperidine-1-carboxylic acid (3,4-dichloro-phenyl)-amide trifluoroacetate 3,4-Dichlorophenyl isocyanate (60mg, 0.319mmol) was added to a stirring solution of 4-[3-(N,N-ditert-butoxycarbonylaminomethyl)phenyl]piperidine (100mg, 0.256mmol) in DCM (5mL) at room temperature. After 16 hours the reaction was quenched with water (5mL) and separated, and extracted the aqueous phase with DCM (5mL). The combined organics were dried over anhydrous sodium sulfate, and concentrated to dryness. The residue was purified by dry flash column chromatography on silica with 50:50, dichloromethane:ethyl acetate. 4-[3-(N,N-di-tertbutoxycarbonylaminomethyl)phenyl]-piperidine-1-carboxylic acid (3,4-dichloro-phenyl)-amide was isolated as a colorless oil, which was dissolved in dichloromethane (25mL), cooled at 0°C, and treated with trifluoroacetic acid (3mL). The reaction mixture was stirred at room temperature under nitrogen for 2 hours, and concentrated to dryness in vacuo. The residue was dissolved in 20% acetonitrile/water [containing 0.1% trifluoroacetic acid] (9mL) and purified by preparative reverse-phase HPLC (C-18, 10 micron reverse-phase column), eluting with 10% to 100% acetonitrile / water (containing 0.1% trifluoroacetic acid). The product fractions were combined and the acetonitrile removed in vacuo. The aqueous residue was frozen and lyophilized to give the title compound as an amorphous white solid (68 mg, 53%). H NMR [(CD₃)₂SO]: δ 8.82 (s, H, NH); 7.88 (s, H); 7.84 (br s, 3H, NH₃⁺); 7.46 (s, H); 7.37-7.22 (m, 5H); 4.24 (br d, 2H); 3.99 (s, 2H); 2.89 (br t, 2H); 2.83-2.70 (m, H); 1.82-1.71 (m, 2H); 1.60-1.44 (m, 2H). MS(Ion spray): 378 and 380 ($M^{+}+1$).

EXAMPLE 352

4-(3-Aminomethyl-phenyl)-piperidine-1-carboxylic acid 2,3-dimethoxybenzylamide-trifluoroacetate.
 (3-Piperidin-4-yl-benzyl) carbamate Wang resin (EXAMPLE 122D) (60μmol) was suspended in dichloromethane (2mL) and added diisopropylethylamine (0.66 mmol) followed by phosgene (0.6

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mmol of a 20% solution in toluene). The reaction mixture was shaken for 5 minutes before washing the resin with toluene (x8). The resin was suspended in DMF (2mL) and to this was added a solution of 2,3-dimethoxybenzylamine (0.6mmol) in DMF (1.5mL) and the reaction mixture shaken for 5 minutes before washing the resin with DMF (x3). The resin was then suspended in dichloromethane (2mL) and treated with TFA (0.5mL). The reaction mixture was shaken for 5 minutes, before the resin was filtered off and the filtrate concentrated to dryness to give the title compound (48μmol) as a pale yellow solid. MS (EI) 383 (M⁺).

By proceeding in a similar manner to the method described in EXAMPLES 351 AND 352, the following compounds set forth in Table 7 were prepared, as the trifluoroacetate salts:

TABLE 7

EG	Structure	M/Z	MS area %	EG	Structure	M/Z	MS area %
353	ZH ₂	391	>95%	354	° → H ~ N ~ N ~ N ~ N ~ N ~ N ~ N ~ N ~ N ~	360	>95%
355		430	>95%	356	O NH,	406	>95%
357		383	>95%	358		436	>95%
359		405	>95%	360		419	>95%
361	NH,	435	>95%	362	NH ₂	423	>95%
363		384	>95%	364	NH ₂	380	>95%
365	O NH2	337	>95%				

IN VITRO TEST PROCEDURE

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Since all the actions of tryptase, as described in the background section, are dependent on its catalytic activity, then compounds that inhibit its catalytic activity will potentially inhibit the actions of tryptase. Inhibition of this catalytic activity may be measured by the in vitro enzyme assay and the cellular assay.

Tryptase inhibition activity is confirmed using either isolated human lung tryptase or recombinant human β tryptase expressed in yeast cells. Essentially equivalent results are obtained using isolated native enzyme or the expressed enzyme. The assay procedure employs a 96 well microplate (Costar 3590) using L-pyroglutamyl-L-prolyl-L-arginine-*para*-nitroanilide (S2366: Quadratech) as substrate (essentially as described by McEuen *et. al.* Biochem Pharm, 1996, 52, pages 331-340). Assays are performed at room temperature using 0.5mM substrate (2 x K_m) and the microplate is read on a microplate reader (Beckman Biomek Plate reader) at 405nm wavelength. The inhibition constant (Ki) for particular compounds of the present invention is set forth in Table 8. It was determined using the procedure set forth herein.

Materials and Methods for Tryptase primary screen (Chromogenic assay)

Assay buffer

50 mM Tris (pH 8.2), 100 mM NaCl, 0.05% Tween 20, 50 ug/ml heparin.

S2366 (Stock solutions of 2.5 mM).

Substrate

Enzyme

Purified recombinant beta Tryptase Stocks of 310 ug/ml.

Protocol (Single point determination)

- Add 60 ul of diluted substrate (final concentration of 500 uM in assay buffer) to each well
 - Add compound in duplicates, final concentration of 20 uM, volume 20 ul
 - Add enzyme at a final concentration of 50 ng/ml in a volume of 20 ul
 - Total volume for each well is 100 ul
 - Agitate briefly to mix and incubate at room temp in the dark for 30 minutes
- Read absorbencies at 405 nM

Each plate has the following controls -

Totals: 60 ul of substrate, 20 ul of buffer (with 0.2% final concentration of DMSO), 20 ul of

35 enzyme

Non-specific: 60 ul of substrate, 40 ul of buffer (with 0.2% DMSO)

Totals:

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60 ul of substrate, 20 ul of buffer (No DMSO), 20 ul of enzyme

Non-specific:

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60 ul of substrate, 40 ul of buffer (No DMSO)

5 Protocol (IC₅₀ and Ki determination)

The protocol is essentially the same as above except that the compound is added in duplicates at the following final concentrations: 0.01, 0.03, 0.1, 0.3, 1, 3, 10 uM (All dilutions carried out manually). For every assay, whether single point or IC50 determination, a standard compound is used to derive IC₅₀ for comparison. From the IC 50 value, the Ki can be calculated using the following formula: Ki = $IC_{50}/(1 + [Substrate]/Km)$.

Using this procedure, Ki values with respect to tryptase for particular compounds of the present invention are set forth in Table 8 below:

TABLE 8

EXAMPLE	NAME	Tryptase Ki (nM)
#		
13	[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(5-phenethyl-	50
	thiophen-2-yl)-methanone hydrochloride	
15	[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(3-	1,070
	phenoxymethyl-phenyl)-methanone hydrochloride)	
18	[4-(5-Aminomethyl-2-methyl-phenyl)-piperidin-1-yl]-(5-	69
	phenethyl-pyridin-3-yl)-methanone di-hydrochloride)	
19	4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-[3-(5-phenyl-	180
	1,3,4-oxadiazol-2-yl)-phenyl]-methanone hydrochloride)	
35	4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-	93
	carbonyl)-piperidine-4-carbonitrile	
36	[4-(3-Aminomethylphenyl)piperidin-1-yl]-(3,4-dichloro-	31
	phenyl)-methanone trifluoroacetate	
48	1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(4-chloro-	390
	phenyl)-methanone trifluoroacetate	
49	1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[5-(2-	390
	chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-methanone	
	trifluoroacetate	
70	1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(4,5,6,7-	290
	tetrahydro-benzo[c]thiophen-1-yl)-methanone-	ŀ
	trifluoroacetate.	
83	1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(4-fluoro-	870
	phenylethynyl)-phenyl]-methanone trifluoroacetate	
92	1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-chloro-	190
	thieno[3,2-b]thiophen-2-yl)-methanone trifluoroacetate	
97	[4-(3-Aminomethylphenyl)-piperidin-1-yl]-(4-phenylethyl-	450
	phenyl)-methanone hydrochloride	
98	[4-(3-Aminomethylphenyl)-piperidin-1-yl]-{3-[2-(2-	180
	hydroxyphenyl)-ethyl]-phenyl)-methanone hydrochloride	
100	[4-(5-Aminomethyl-thiophen-2-yl)-piperidin-1-yl]-(5-	490
	phenylethyl-pyridin-3-yl)-methanone di-hydrochloride	
EXAMPLE#	NAME	Tryptase Ki (nM)

13	[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(5-phenethyl-thiophen-	50
	2-yl)-methanone hydrochloride	<u> </u>
15	[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-(3-phenoxymethyl-	1,070
	phenyl)-methanone hydrochloride)	
18	[4-(5-Aminomethyl-2-methyl-phenyl)-piperidin-1-yl]-(5-phenethyl-	69
	pyridin-3-yl)-methanone di-hydrochloride)	
35	4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-	93
	piperidine-4-carbonitrile	
48	1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(4-chloro-phenyl)-	390
	methanone trifluoroacetate	
49	1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[5-(2-chloro-	390
	phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-methanone trifluoroacetate	
70	1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(4,5,6,7-	290
	tetrahydro-benzo[c]thiophen-1-yl)-methanone-trifluoroacetate.	
83	1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(4-fluoro-	870
	phenylethynyl)-phenyl]-methanone trifluoroacetate	
92	1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5-chloro-	190
	thieno[3,2-b]thiophen-2-yl)-methanone trifluoroacetate	
97	[4-(3-Aminomethylphenyl)-piperidin-1-yl]-(4-phenylethyl-phenyl)-	450
	methanone hydrochloride	
98	[4-(3-Aminomethylphenyl)-piperidin-1-yl]-{3-[2-(2-	180
	hydroxyphenyl)-ethyl]-phenyl)-methanone hydrochloride	
100	[4-(5-Aminomethyl-thiophen-2-yl)-piperidin-1-yl]-(5-phenylethyl-	490
	pyridin-3-yl)-methanone di-hydrochloride	

This data clearly shows that compounds of the present invention exhibit tryptase inhibition activity. Consequently, compounds of the present invention readily have applications in pharmaceutical compositions for treating a wide variety of tryptase related conditions, and naturally, in methods for treating such conditions in patients.

The present invention is not to be limited in scope by the specific embodiments describe herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and the accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

Various publications are cited herein, the disclosures of which are incorporated by reference in their entireties.

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group is beta to the

WHAT IS CLAIMED IS:

1. A compound of formula (I):-

R¹ NH

5 such that Ar is an aryl group or a heteroaryl group, and the

group on the arvl.

wherein:-

is a single or a double bond;

10 R¹ and R² are each independently hydrogen or lower alkyl;

 R^3 is aryl, arylalkenyl, cycloalkenyl, cycloalkyl, heteroaryl, heteroarylalkenyl, heterocycloalkenyl, a carbon linked heterocycloalkyl or alkyl optionally substituted by one or more groups selected from hydroxy, alkoxy, alkyloxycarbonylamino, cycloalkyl, heterocycloalkyl, R^6 , $-OR^6$, $-S(O)_mR^6$ or $-C(=O)-R^6$;

R⁴ is hydrogen, acyl, alkoxy, alkyloxycarbonyl, carboxy, cyano, halo, hydroxy, -C(=O)-NY¹Y² or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, hydroxy, -S(O)_m-alkyl or -NY¹Y²;

 R^5 is hydrogen, acyl, alkoxy, alkyloxycarbonyl, aryl, carboxy, cyano, halo, heteroaryl, heteroaryloxy, heterocycloalkyl, heterocycloalkyloxy, heterocycloalkyloxy, heteroarylalkyloxy, hydroxy,

trifluoromethyl, -C(=O)-NY¹Y², -NY¹Y², -Z¹-C₂₋₆alkylene-R⁷ or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, aryl, heteroaryl, heterocycloalkyl, hydroxy, ureido, -C(=O)-NY¹Y², -SO₂-NY¹Y², -S(O)_m-alkyl or -NY¹Y²;

R⁶ is aryl or heteroaryl;

R⁷ is hydroxy, alkoxy, ureido, -C(=O)-NY¹Y², -SO₂-NY¹Y², -S(O)_m-alkyl or -NY¹Y²;

25 R⁸ is hydrogen or lower alkyl;

 Y^1 and Y^2 are independently hydrogen, alkenyl, alkyl, aryl, arylalkyl, cycloalkyl, heteroaryl, heteroarylalkyl or heterocycloalkyl; or the group -NY 1 Y 2 may form a cyclic amine;

 Z^1 is O, S(O)_m or NR⁸;

m is zero or an integer 1 to 2;

5 n is zero or an integer 1 to 4;

an N-oxide of said compound, a prodrug of said compound, a pharmaceutically acceptable salt of said compound, a solvate of said compound, and a hydrate of said compound.

- 2. The compound of Claim 1, wherein R¹ and/or R² is hydrogen, and R³ is an aryl or an heteroaryl.
 - 3. The compound of Claim 2, wherein said R³ aryl comprises a phenyl or a naphthyl.
 - 4. The compound of Claim 2, wherein said R³ aryl is substituted with at least one substituent.
 - 5. The compound of Claim 4, wherein said substituent is selected from the group consisting of a halo atom, an alkyl substituted by aryl, an alkyl substituted by aryloxy, an alkyl substituted by arylakynyl, an arylaky
 - 6. The compound of Claim 5, wherein said aryl or heteroaryl of said substituent is further substituted by at least one aryl group substituent.
- 7. The compound of Claim 2, wherein said heteroaryl comprises a pyridyl, a quinolinyl, a thienyl, a furanyl, or an indolyl.
 - 8. The compound of Claim 7, wherein said heteroaryl is substituted with at least one substituent.
- 9. The compound of Claim 8, wherein said substituent comprises an alkyl, an alkyl substituted by an aryl, an alkyl substituted by an aryloxy, an alkyl substituted by an arylalkynyl, an arylalkynyl, a heteroaryl, an arylalkenyl or an arylalkyoxy.
 - 10. The compound of Claim 9, wherein said aryl of said substituent is further substituted by at least one aryl substituent.
 - 11. The compound of Claim 1, wherein R⁴ comprises hydrogen or a cyano group.

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- 12. The compound of Claim 1, wherein R⁵ comprises a hydrogen, a lower alkyl, or a halo.
- 13. The compound of Claim 1, wherein ---- is a single bond.

- 14. The compound of Claim 1, wherein n=2.
- 15. The compound of Claim 1, wherein:

Ar comprises a phenyl group;

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 $R^1 = R^2 = hydrogen;$

R³ comprises an aryl, a naphthyl, or a heteroaryl;

R⁴ comprises hydrogen or a cyano group;

R⁵ comprises hydrogen, a lower alkyl, or a halo;

-----represents a single bond; and

n=2.

- 16. The compound of Claim 15, wherein said aryl or said naphthyl of R³ is substituted with at least one substituent comprising a halo atom, an alkyl substituted by aryl, an alkyl substituted by aryloxy, an alkyl substituted by aroyl, an alkyl substituted by aroyl, an alkyl substituted by aroyl, an arylalkynyl, an a
- 17. The compound of Claim 16, wherein said aryl or said heteroaryl of said substituent is further substituted by at least one aryl substituent.

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- 18. The compound of Claim 15, wherein said heteroaryl of R³ is substituted by at least one substituent comprising a pyridyl, a quinolinyl, a thienyl a furanyl, or an indolyl.
- 19. The compound of Claim 18, wherein said substituent of said heteroaryl is further substituted by at least one moiety comprising an alkyl substituted by an aryl, an alkyl substituted by an aryloxy, an alkyl substituted by an aroyl, an alkyl substituted heteroaryl, an arylalkynyl, a heteroaryl, an arylalkynyl, or an arylalkyloxy.
 - 20. The compound of Claim 19, wherein an aryl of said moiety is further substituted by at least one aryl substituent.
 - 21. A compound of formula (Ia):

wherein

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R³ is aryl, arylalkenyl, cycloalkenyl, cycloalkyl, heteroaryl, heteroarylalkenyl, heterocycloalkenyl, a carbon linked heterocycloalkyl or alkyl optionally substituted by one or more groups selected from hydroxy, alkyloxycarbonylamino, cycloalkyl, heterocycloalkyl, R⁶, -OR⁶, -S(O)_mR⁶ or -C(=O)-R⁶;

R⁴ is hydrogen, acyl, alkoxy, alkyloxycarbonyl, carboxy, cyano, halo, hydroxy, -C(=O)-NY¹Y² or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, hydroxy, -S(O)_m-alkyl or -NY¹Y²; and

 R^5 is hydrogen, acyl, alkoxy, alkyloxycarbonyl, aryl, carboxy, cyano, halo, heteroaryl, heteroaryloxy, heterocycloalkyl, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroarylalkyloxy, hydroxy, trifluoromethyl, $-C(=O)-NY^1Y^2$, $-NY^1Y^2$, $-Z^1-C_{2-6}$ alkylene- R^7 or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, aryl, heteroaryl, heterocycloalkyl, hydroxy, ureido, $-C(=O)-NY^1Y^2$, $-SO_2-NY^1Y^2$, $-S(O)_m$ -alkyl or $-NY^1Y^2$, and,

a corresponding N-oxide of said compound, a prodrug of said compound, a pharmaceutically acceptable salt of said compound, a solvate of said compound, an N-oxides and prodrugs.

- 20 22. The compound of Claim 21, wherein R³ is an aryl comprising a phenyl or a naphthyl.
 - 23. The compound of Claim 22, wherein said aryl is substituted by at least one substituent comprising a halo atom, an alkyl substituted by an aryl, an alkyl substituted by a heteroaryl.

- 24. The compound of Claim 23, wherein said aryl or heteroaryl of said substituent is further substituted by at least one aryl group substituent.
- 5 25. The compound of Claim 21, wherein R³ comprises phenylC₁₋₃alkylpyridyl [e.g. 5-phenylethyl-pyrid-3-yl], phenylC₁₋₃alkylthienyl [e.g. 5-phenylethyl-thien-2-yl] or indolyl [e.g. indol-6-yl].
- 26. The compound of Claim 21, wherein R³ is a heteroaryl comprising a pyridyl, a quinolinyl, a thienyl, a furanyl, or an indolyl.
 - 27. The compound of Claim 26, wherein said heteroaryl is substituted by at least one substituent comprising an alkyl substituted by an aryl, or an alkyl substituted by a heteroaryl.
- 15 28. The compound of Claim 27, wherein said aryl and said heteroaryl of said substituent are further substituted by at least one aryl group substituent.
 - 29. The compound of Claim 28, wherein R³ comprises phenylC₁₋₃alkylpyridyl [e.g. 5-phenylethyl-pyrid-3-yl], phenylC₁₋₃alkylthienyl [e.g. 5-phenylethyl-thien-2-yl], or indolyl [e.g. indol-6-yl].
 - 30. The compound of Claim 21, wherein R⁴ comprises a hydrogen or a cyano.
 - 31. The compound of Claim 21, wherein R⁵ comprises a hydrogen, a lower alkyl or a halo.
 - 32. The compound of Claim 31, wherein R⁵ comprises a methyl or a fluoro.
 - 33. The compound of Claim 31, wherein R⁵ is attached to the phenyl ring of formula (Ia) in the position para to the CH₂NH₂ group.
 - 34. The compound of Claim 21, wherein:

R³ is a phenyl, a naphthyl, a heteroaryl selected from the group consisting a pyridyl, a quinolinyl, a thienyl, a furanyl, and an indolyl, a phenyl substituted by at least one substituent, a naphthyl substituted by at least one substituent, or a heteroaryl selected from the group consisting a pyridyl, a quinolinyl, a thienyl, a furanyl, and an indolyl, that is substituted by at least one substituent,

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wherein said substituent is selected from the group consisting of a halo atom, an alkyl substituted by aryl, and alkyl substituted heteroaryl, wherein the aryl or heteroaryl groups are further substituted by one or more aryl group substituents;

R⁴ comprises hydrogen or a cyano; and

R⁵ comprises hydrogen, a lower alkyl or a halo.

35. The compound of Claim 34, wherein:

R³ comprises phenylC₁₋₃alkylpyridyl [e.g. 5-phenylethyl-pyrid-3-yl], phenylC₁₋₃alkylthienyl [e.g. 5-phenylethyl-thien-2-yl] or indolyl [e.g. indol-6-yl;

R⁴ comprises a hydrogen or a cyano; and

R⁵ comprises a methyl or a fluoro, and is attached to the phenyl ring of formula (Ib) in the position para to the CH₂NH₂ group.

36. A compound of formula (Ib):

R³ O R⁴ 1 2 CH₂NH₂ (Ib

wherein

R³ is aryl, arylalkenyl, cycloalkenyl, cycloalkyl, heteroaryl, heteroarylalkenyl, heterocycloalkenyl, a carbon linked heterocycloalkyl or alkyl optionally substituted by one or more groups selected from hydroxy, alkoxy, alkyloxycarbonylamino, cycloalkyl, heterocycloalkyl, R⁶, -OR⁶, -S(O)_mR⁶ or -C(=O)-R⁶;

 R^4 is hydrogen, acyl, alkoxy, alkyloxycarbonyl, carboxy, cyano, halo, hydroxy, $-C(=O)-NY^1Y^2$ or alkyl optionally substituted with alkoxy, alkylcarbonylamino, alkylsulfonylamino, hydroxy,

25 $-S(O)_m$ -alkyl or $-NY^1Y^2$; and

 R^5 is hydrogen, acyl, alkoxy, alkyloxycarbonyl, aryl, carboxy, cyano, halo, heteroaryl, heteroaryloxy, heterocycloalkyl, heterocycloalkyloxy, heterocycloalkylalkyloxy, heteroarylalkyloxy, hydroxy, trifluoromethyl, $-C(=O)-NY^1Y^2$, $-NY^1Y^2$, $-Z^1-C_{2-6}$ alkylene- R^7 or alkyl optionally substituted with

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- alkoxy, alkylcarbonylamino, alkylsulfonylamino, aryl, heteroaryl, heterocycloalkyl, hydroxy, ureido, $-C(=O)-NY^1Y^2$, $-SO_2-NY^1Y^2$, $-S(O)_m$ -alkyl or $-NY^1Y^2$, and,
- a corresponding N-oxide of said compound, a prodrug of said compound, a pharmaceutically acceptable salt of said compound, a solvate of said compound, an N-oxides and prodrugs.
- 37. The compound of Claim 36, wherein R³ is an aryl comprising a phenyl or a naphthyl.
- 38. The compound of Claim 37, wherein said aryl is substituted by at least one substituent comprising a halo atom, an alkyl substituted by an aryl, an alkyl substituted by a heteroaryl.
- 39. The compound of Claim 38, wherein said aryl or heteroaryl of said substituent is further substituted by at least one aryl group substituent.
- 40. The compound of Claim 36, wherein R³ is a heteroaryl comprising a pyridyl, a quinolinyl, a thienyl, a furanyl, or an indolyl.
 - 41. The compound of Claim 41, wherein said heteroaryl is substituted by at least one substituent comprising an alkyl substituted by an aryl, or an alkyl substituted by a heteroaryl.
- 42. The compound of Claim 42, wherein said aryl and said heteroaryl of said substituent are further substituted by at least one aryl group substituent.
 - 43. The compound of Claim 36, wherein R³ comprises phenylC₁₋₃alkylpyridyl [e.g. 5-phenylethyl-pyrid-3-yl], phenylC₁₋₃alkylthienyl [e.g. 5-phenylethyl-thien-2-yl], or indolyl [e.g. indol-6-yl].
 - 44. The compound of Claim 36, wherein R⁴ comprises a hydrogen or a cyano.
 - 45. The compound of Claim 36, wherein R⁵ comprises a hydrogen, a lower alkyl or a halo.
- 30 46. The compound of Claim 45, wherein R⁵ comprises a methyl or a fluoro.
 - 47. The compound of Claim 45, wherein R⁵ is attached to the phenyl ring of formula (Ib) in the position para to the CH₂NH₂ group.
- 35 48. The compound of Claim 36, wherein:

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R³ is a phenyl, a naphthyl, a heteroaryl selected from the group consisting a pyridyl, a quinolinyl, a thienyl, a furanyl, and an indolyl, a phenyl substituted by at least one substituent, a naphthyl substituted by at least one substituent, or a heteroaryl selected from the group consisting a pyridyl, a quinolinyl, a thienyl, a furanyl, and an indolyl, that is substituted by at least one substituent,

wherein said substituent is selected from the group consisting of a halo atom, an alkyl substituted by aryl, and alkyl substituted heteroaryl, wherein the aryl or heteroaryl groups are further substituted by one or more aryl group substituents;

R⁴ comprises hydrogen or a cyano; and

R⁵ comprises hydrogen, a lower alkyl or a halo.

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49. The compound of Claim 48, wherein:

R³ comprises phenylC₁₋₃alkylpyridyl [e.g. 5-phenylethyl-pyrid-3-yl], phenylC₁₋₃alkylthienyl [e.g. 5-phenylethyl-thien-2-yl] or indolyl [e.g. indol-6-yl;

R⁴ comprises a hydrogen or a cyano; and

 R^{5} comprises a methyl or a fluoro, and is attached to the phenyl ring of formula (Ib) in the position para to the $CH_{2}NH_{2}$ group.

- 50. The compound of Claim 1, selected from the group consisting of:
- 3-[1-(5-phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine;
- 3-[1-(3-phenylethyl-benzoyl)-piperidin-4-yl]-benzylamine;
 - 3-{1-[3-(4-hydroxyphenyl)ethyl-benzoyl]-piperidin-4-yl}-benzylamine;
 - 3-{1-[3-(6-amino-pyridin-3-yl)ethyl-benzoyl]-piperidin-4-yl}-benzylamine;
 - 3-[1-(5-phenylethyl-thiophene-2-carbonyl)-piperidin-4-yl]-benzylamine;
 - 4-fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine;
- 4-methyl-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine;
 - 3-[1-(indole-6-carbonyl)-piperidin-4-yl]-benzylamine;
 - 4-(3-aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-4-carbonitrile
 - [4-(3-aminomethylphenyl)piperidin-1-yl]-(3,4-dichlorophenyl)methanone;
 - $1-\{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl\}-3-methylsulfanyl-6,7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl\}-3-methylsulfanyl-6,7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl\}-3-methylsulfanyl-6,7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-methylsulfanyl-6,7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-methylsulfanyl-6,7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-methylsulfanyl-6,7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-methylsulfanyl-6,7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl]-3-methylsulfanyl-6,7-dihydro-5H-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-[4-(3-Aminomethyl-phenyl)-piperidin$
- 30 benzo[c]thiophen-4-one trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-methylsulfanyl-6,7-dihydro-benzo[c]thiophen-1-yl)-methanone trifluoroacetate;
 - 1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-ethylsulfanyl-6,6-dimethyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate;
- 35 1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-propylsulfanyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate;

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1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-isopropylsulfanyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate;

- 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-benzo[b]thiophen-2-yl-methanone-trifluoroacetate;
- 1-[4-(3-Aminomethyl-phenyl)-4-hydroxy-piperidin-1-yl]-1-(5-phenethyl-pyridin-3-yl)-methanone-
- 5 ditrifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(1-methyl-1H-indol-3-yl)-methanone-trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(2-fluoro-phenylethynyl)-phenyl]-methanone trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[2-(2-fluoro-phenyl)-ethyl]-phenyl}-methanone trifluoroacetate:
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[2-(6-amino-pyridin-3-yl)-ethyl]-phenyl}-methanone tri-trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(6-chloro-thieno[3,2-b]thiophen-2-yl)-methanone trifluoroacetate;
- 15 (3R,4S) and (3S, 4R)-4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester dihydrochloride;
 - 3-[1-(5-Phenylethynyl-furan-2-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate;
 - 4-(3-Aminomethyl-phenyl)-piperidine-1-carboxylic acid (3,4-dichloro-phenyl)-amide trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(2,3-dihydro-benzofuran-5-yl)-methanone;
- 20 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5,6-dichloro-pyridin-3-yl)-methanone;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-bromo-4-fluoro-phenyl)-methanone;
 - (E)-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-(2-nitro-phenyl)-propenone;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-bromo-5-iodo-phenyl)-methanone; and
 - (E)-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-phenyl-propenone.

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- 51. A pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier thereof.
- 52. The pharmaceutical composition of Claim 51, wherein said compound is selected from the group consisting of:
- 3-[1-(5-phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine;
- 3-[1-(3-phenylethyl-benzoyl)-piperidin-4-yl]-benzylamine;
- 3-{1-[3-(4-hydroxyphenyl)ethyl-benzoyl]-piperidin-4-yl}-benzylamine;
- 3-{1-[3-(6-amino-pyridin-3-yl)ethyl-benzoyl]-piperidin-4-yl}-benzylamine;
- 35 3-[1-(5-phenylethyl-thiophene-2-carbonyl)-piperidin-4-yl]-benzylamine;
 - 4-fluoro-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine;
 - 4-methyl-3-[1-(5-phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzylamine;

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- 3-[1-(indole-6-carbonyl)-piperidin-4-yl]-benzylamine;
- 4-(3-aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-4-carbonitrile
- [4-(3-aminomethylphenyl)piperidin-1-yl]-(3,4-dichlorophenyl)methanone;
- 1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-methylsulfanyl-6,7-dihydro-5H-
- 5 benzo[c]thiophen-4-one trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-methylsulfanyl-6,7-dihydro-benzo[c]thiophen-1-yl)-methanone trifluoroacetate;
 - 1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-ethylsulfanyl-6,6-dimethyl-6,7-dihydro-5H-benzoschiophen-4-one trifluoroacetate;
- 1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-propylsulfanyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate;
 - 1-{1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-methanoyl}-3-isopropylsulfanyl-6,7-dihydro-5H-benzo[c]thiophen-4-one trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-benzo[b]thiophen-2-yl-methanone-trifluoroacetate;
- 15 1-[4-(3-Aminomethyl-phenyl)-4-hydroxy-piperidin-1-yl]-1-(5-phenethyl-pyridin-3-yl)-methanone-ditrifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(1-methyl-1H-indol-3-yl)-methanone-trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-[3-(2-fluoro-phenylethynyl)-phenyl]-methanone trifluoroacetate;
- 20 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[2-(2-fluoro-phenyl)-ethyl]-phenyl}-methanone trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-{3-[2-(6-amino-pyridin-3-yl)-ethyl]-phenyl}-methanone tri-trifluoroacetate;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(6-chloro-thieno[3,2-b]thiophen-2-yl)-methanone trifluoroacetate;
 - (3R,4S) and (3S, 4R)-4-(3-Aminomethyl-phenyl)-1-(5-phenethyl-pyridine-3-carbonyl)-piperidine-3-carboxylic acid ethyl ester dihydrochloride;
 - 3-[1-(5-Phenylethynyl-furan-2-carbonyl)-piperidin-4-yl]-benzylamine trifluoroacetate;
 - 4-(3-Aminomethyl-phenyl)-piperidine-1-carboxylic acid (3,4-dichloro-phenyl)-amide trifluoroacetate;
- 30 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(2,3-dihydro-benzofuran-5-yl)-methanone;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(5,6-dichloro-pyridin-3-yl)-methanone;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-bromo-4-fluoro-phenyl)-methanone;
 - (E)-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-(2-nitro-phenyl)-propenone;
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-1-(3-bromo-5-iodo-phenyl)-methanone;
- 35 (E)-1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-phenyl-propenone; and
 - 1-[4-(3-Aminomethyl-phenyl)-piperidin-1-yl]-3-cyclohexyl-propan-1-one.

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- 53. A pharmaceutical composition comprising a compound of Claim 21 and a pharmaceutically acceptable carrier thereof.
- 54. A pharmaceutical composition comprising a compound of Claim 36 and a pharmaceutically acceptable carrier thereof.
 - A method for treating a patient suffering from, or subject to, a condition that can be ameliorated by the administration of an inhibitor of tryptase, wherein the method comprises administering to the patient an effective amount of a compound of Claim 1.

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- 56. The method of Claim 55, wherein the condition comprises inflammatory disease, a disease of joint cartilage destruction, ocular conjunctivitis, vernal conjunctivitis, inflammatory bowel disease, asthma, allergic rhinitis, an interstitial lung disease, fibrosis, sceleroderma, pulmonary fibrosis, liver cirrhosis, myocardial fibrosis, a neurofibroma, a hypertrophic scar, a dermatological condition, a condition related to atherosclerotic plaque rupture, periodontal disease, diabetic retinopathy, tumor growth, anaphylaxis, multiple sclerosis, a peptic ulcer, or a syncytial viral infection.
- 57. The method of Claim 56, wherein the inflammatory disease comprises joint inflammation,
 20 arthritis, rheumatoid arthritis, rheumatoid spondylitis, gouty arthritis, traumatic arthritis,
 rubella arthritis, psoriatic arthritis, or osteoarthritis;
 the dermatological condition comprises atopic dermatitis or psoriasis; and
 the condition related to atherosclerotic plaque rupture comprises myocardial infarction, stroke,
 or angina.

- A method for treating a patient suffering from, or subject to, a condition that can be ameliorated by the administration of an inhibitor of tryptase, wherein the method comprises administering to the patient an effective amount of a compound of Claim 21.
- The method of Claim 58, wherein the condition comprises inflammatory disease, a disease of joint cartilage destruction, ocular conjunctivitis, vernal conjunctivitis, inflammatory bowel disease, asthma, allergic rhinitis, an interstitial lung disease, fibrosis, sceleroderma, pulmonary fibrosis, liver cirrhosis, myocardial fibrosis, a neurofibroma, a hypertrophic scar, a dermatological condition, a condition related to atherosclerotic plaque rupture, periodontal disease, diabetic retinopathy, tumor growth, anaphylaxis, multiple sclerosis, a peptic ulcer, or a syncytial viral infection.

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- 60. The method of Claim 59, wherein the inflammatory disease comprises joint inflammation, arthritis, rheumatoid arthritis, rheumatoid spondylitis, gouty arthritis, traumatic arthritis, rubella arthritis, psoriatic arthritis, or osteoarthritis; the dermatological condition comprises atopic dermatitis or psoriasis; and the condition related to atherosclerotic plaque rupture comprises myocardial infarction, stroke, or angina.
- A method for treating a patient suffering from, or subject to, a condition that can be ameliorated by the administration of an inhibitor of tryptase, wherein the method comprises administering to the patient an effective amount of a compound of Claim 36.
 - 62. The method of Claim 61, wherein the condition comprises inflammatory disease, a disease of joint cartilage destruction, ocular conjunctivitis, vernal conjunctivitis, inflammatory bowel disease, asthma, allergic rhinitis, an interstitial lung disease, fibrosis, sceleroderma, pulmonary fibrosis, liver cirrhosis, myocardial fibrosis, a neurofibroma, a hypertrophic scar, a dermatological condition, a condition related to atherosclerotic plaque rupture, periodontal disease, diabetic retinopathy, tumor growth, anaphylaxis, multiple sclerosis, a peptic ulcer, or a syncytial viral infection.
- The method of Claim 62, wherein the inflammatory disease comprises joint inflammation, arthritis, rheumatoid arthritis, rheumatoid spondylitis, gouty arthritis, traumatic arthritis, rubella arthritis, psoriatic arthritis, or osteoarthritis; the dermatological condition comprises atopic dermatitis or psoriasis; and the condition related to atherosclerotic plaque rupture comprises myocardial infarction, stroke, or angina.
 - 64. A pharmaceutical composition comprising a compound of Claim 1 and a second compound selected from the group consisting of a beta andrenergic agonist, an anticholinergic, an anti-inflammatory corticosteroid, and an anti-inflammatory agent; and a pharmaceutically acceptable carrier thereof.
- The pharmaceutical composition of Claim 64, wherein the beta andrenergic agonist comprises albuterol, terbutaline, formoterol, fenoterol or prenaline;
 the anti-cholinergic comprises ipratropium bromide;
 the anti-inflammatory corticosteroid comprises beclomethasone dipropionate, triamcinolone acetonide, flunisolide or dexamethasone; and
 the anti-inflammatory agent comprises sodium cromoglycate or nedocromil sodium.

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A pharmaceutical composition comprising a compound of formula 21 and a second compound selected from the group consisting of a beta andrenergic agonist, an anticholinergic, an anti-inflammatory corticosteroid, and an anti-inflammatory agent; and a pharmaceutically acceptable carrier thereof.

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67. The pharmaceutical composition of im 66, wherein the beta andrenergic agonist comprises albuterol, terbutaline, formoterol, fenoterol or prenaline; the anti-holinergic comprises ipratropium bromide; the anti-inflammatory corticosteroid comprises beclomethasone dipropionate, triamcinolone acetonide, flunisolide or dexamethasone; and the anti-inflammatory agent comprises sodium cromoglycate or nedocromil sodium.

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A pharmaceutical composition comprising a compound Claim 36 and a second compound selected from the group consisting of a beta andrenergic agonist, an anticholinergic, an anti-inflammatory corticosteroid, and an anti-inflammatory agent; and a pharmaceutically acceptable carrier thereof.

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69. The pharmaceutical composition of Claim 66, wherein the beta andrenergic agonist comprises albuterol, terbutaline, formoterol, fenoterol or prenaline; the anticholinergic comprises ipratropium bromide; the anti-inflammatory corticosteroid comprises beclomethasone dipropionate, triamcinolone acetonide, flunisolide or dexamethasone; and the anti-inflammatory agent comprises sodium cromoglycate or nedocromil sodium.

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70. A method for treating a patient suffering from asthma, comprising administering to the patient a combination of a compound of Claim 1, and a second compound selected from the group consisting of a beta andrenergic agonist, an anticholinergic, an anti-inflammatory corticosteroid, and an anti-inflammatory agent

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71.

A method for treating a patient suffering from asthma, comprising administering to the patient a combination of a compound of Claim 21, and a second compound selected from the group consisting of a beta andrenergic agonist, an anti-holinergic, an anti-inflammatory corticosteroid, and an anti-inflammatory agent.

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72. A method for treating a patient suffering from asthma, comprising administering to the patient a combination of a compound of Claim 36, and a second compound selected from the group

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consisting of a beta andrenergic agonist, an anticholinergic, an anti-inflammatory corticosteroid, and an anti-inflammatory agent.

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INTERNATIONAL SEARCH REPORT

Int ional Application No PCT/US 01/13811

A CLASSII	FICATION OF SUBJECT MATTER					
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	CO7D405/06 CO7D513/04 CO7D413/1					
•	CO7D401/12 CO7D487/04 CO7D417/0	06 CO7D471/O4 CO7D40	05/14			
According to	International Patent Classification (IPC) or to both national classificat	ion and iPC				
B. FIELDS SEARCHED						
Minimum documentation searched (classification system followed by classification symbols)						
IPC 7						
Documentat	ion searched other than minimum documentation to the extent that su	ch documents are included in the fields sear	ched			
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Electronic da	ata base consulted during the international search (name of data base	e and, where practical, search terms used)				
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C. DOCUME	ENTS CONSIDERED TO BE RELEVANT					
Category °	Citation of document, with indication, where appropriate, of the rele	vant passages	Relevant to claim No.			
Λ	BURGESS L E: "MAST CELL TRYPTASE	A	1			
Α	TARGET FOR DRUG DESIGN"	AS A				
	DRUG NEWS AND PERSPECTIVES,					
	vol. 13, no. 3, 2000, pages 147-1	57				
	XP000986039					
	ISSN: 0214-0934	1				
	* Compounds 1-20 *		•			
						
Α	DE 44 07 139 A (THOMAE GMBH DR K)		1			
	7 September 1995 (1995-09-07)		•			
	* Formula I *					
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L Furt	her documents are listed in the continuation of box C.	X Patent family members are listed in	annex.			
° Special ca	itegories of cited documents:	Til later decument published effects in the	-Ai			
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consid	dered to be of particular relevance	cited to understand the principle or theo invention	ry underlying the			
"E" earlier of	document but published on or after the international late	X* document of particular relevance; the cla				
"L* document which may throw doubts on priority claim(s) or involve an inventive step when the document is taken alone			iment is taken alone			
citatio	n or other special reason (as specified)	'Y' document of particular relevance; the cla cannot be considered to involve an inve				
	ent referring to an oral disclosure, use, exhibition or means	document is combined with one or more ments, such combination being obvious	other such docu-			
"P" docume	ent published prior to the international filing date but	in the art.	·			
later ti	han the priority date claimed	'&" document member of the same patent fa	mily			
Date of the	actual completion of the international search	Date of mailing of the international sear	ch report			
	1 7 7 0001	05/07/0001				
1	1 July 2001	26/07/2001				
Name and	mailing address of the ISA	Authorized officer				
	European Patent Office, P.B. 5818 Patentlaan 2					
	NL - 2280 HV Rijswijk *el. (+31-70) 340-2040, Tx. 31 651 epo nl, Fay: (+31-70) 340-2016 Johnson, C					
	Fax: (+31-70) 340-3016	oonnson, c				

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

In snal Application No PCT/US 01/13811

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07D405/10 A61K31/451 A61P29/0						
According to International Patent Classification (IPC) or to both national classification	ation and IPC					
B. FIELDS SEARCHED						
Minimum documentation searched (classification system followed by classification	on symbols)					
Documentation searched other than minimum documentation to the extent that s	uch documents are included in the fields coorded					
Documentation scarcing outer than similaring documentation to the extent that o	our documents are included in the fields searched					
Electronic data base consulted during the international search (name of data base	Electronic data base consulted during the international search (name of data base and, where practical, search terms used)					
C. DOCUMENTS CONSIDERED TO BE RELEVANT						
Category Citation of document, with indication, where appropriate, of the rele	evant passages Relevant to claim No.					
Further documents are listed in the continuation of box C.	χ Patent family members are listed in annex.					
Special categories of cited documents:	'T' later document published after the international filing date					
"A" document defining the general state of the art which is not considered to be of particular relevance	or priority date and not in conflict with the application but cited to understand the principle or theory underlying the					
"E" earlier document but published on or after the international filing date	invention "X" document of particular relevance; the claimed invention					
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another	cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone					
citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the					
O' document referring to an oral disclosure, use, exhibition or other means	document is combined with one or more other such docu- ments, such combination being obvious to a person skilled					
P document published prior to the international filing date but later than the priority date claimed	in the art. *&* document member of the same patent family					
Date of the actual completion of the international search	Date of mailing of the international search report					
11 July 2001						
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2	Authorized officer					
NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,	1					
Fax: (+31-70) 340-3016	Johnson, C					

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-49,51,53-72 (all part)

Present claims 1-49,51,53-72 relate to compounds defined by reference to a desirable characteristic or property, namely prodrugs. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds of Formula (I), their N-oxides. pharmaceutically acceptable salts, solvates and hydrates.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Ini onal Application No PCT/US 01/13811

Patent document cited in search report Publication date Patent family member(s) Publication date DE 4407139 A 07-09-1995 NONE	
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